ACTA OPHTHALMOLOGICA

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CONGRESSUS XIX OPHTHALMICORUM SEPTENTRIONALIUM

XIX MEETING OF NORDIC OPHTHALMOLOGISTS

held in Bergen June 18th to 21st 1969

OFFICIAL TRANSACTIONS

(Edited by *H Aasved* Bergen)

Thursday June 19th

Friday June 20th

Saturday June 19st

Film program

General Meeting

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1970

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Acta had a precursor in the nineteenth century Nordisk ophthalmologisk Tidsskrift Since however this periodical was written in the Scandinavian languages it could not expect any wide circulation and indeed it ran for only a few years At that time Scandinavian ophthalmologists had to send their papers for publication to foreign journals which involved various difficulties Scandinavian thinking characteristics and tradition were often lost more or less in the adaptation of the publications to the demands of a foreign editorial board To this very day several renowned Scandinavian ophthalmologists are believed to be English French or German because their papers were published in journals of these nationalities

Acta Ophthalmologica is owned by the ophthalmological societies of the Scandinavian countries and its editors are appointed by these societies Quite naturally Acta Ophthalmologica is therefore primarily a forum for Scandinavian publications but in the course of time many authors from other countries have found their way to its columns

Anyone who has tried must admit that it is by no means easy to present one s thoughts in a foreign language Even with the aid of translators it is difficult to preserve subtle differences and to avoid errors entirely The editors must still trust in the readers indulgence but will make every effort to do better

The editing of Acta Ophthalmologica has always been characterized by tolerance Censorship in science is just as unattractive as it is in politics Whether an author s views coincide with those of the editorial board or with expert opinion is immaterial Of course the editors must call attention to downright errors or defects but without rejecting a new idea or an original observation I

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Formally too it has been endeavoured to present each contribution with the author's personality characteristics preserved as far as at all possible Pressing the papers into a given pattern might perhaps facilitate the work for the printer librarian and reviewer but it does not always promote the desire for reading

If a person's publications are to be assessed as a basis for an appointment to a post official or honorary it is naturally of the utmost importance that they be correct and flawless In an editorial evaluation the main thing is whether a paper brings something of value In science it is positivity which counts Fruitful ideas observations and experiments do not lose their value merely because they are presented in an unsatisfactory way The editorial board should not play the part of a schoolmaster discouraging the contributors Even a demand as simple as a given rigid system of listing references may seem almost prohibitive to writers in far away places

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For the tribute rendered by my co editors by dedicating without my knowledge fascicle 3 to me on occasion of my 70th birthday I want to express my sincere thanks to all contributors and my cordial forgiveness to my friends on the editorial board

Holger Ehlers
Ex editor

From the Departments of Ophthalmology and Pathology Hacettepe University Medical Faculty Ankara Turkey

HISTOCHEMICAL INVESTIGATIONS ON LIGNEOUS CONJUNCTIVITIS AND A NEW METHOD OF TREATMENT

BY

TANJU FIRAT and BEHÇET TINAZTEPE

Ligneous conjunctivitis is one of the rare forms of membraneous conjunctivitis This chronic recurrent and somewhat peculiar form of conjunctivitis was first described by *Lijo Pavia* in 1924 *Morax* (1928) made the first anatomo patho logic investigation and used the term granuloma In 1935 Borel introduced the term ligneous conjunctivitis *Duke Elder* (1965) found about 50 cases in opthalmic literature

Ligneous conjunctivitis is rarely unilateral affecting girls more than boys It causes severe corneal complications which usually end with perforation and quite often the loss of both eyes

The membrane is hard and may be 1 or 2 mm thick Haemorrhages occur when removal is attempted and they reform within a few days thicker than before No specific microorganisms cultivated

Treatment was uneffective and the etiology was unknown (*Duke Elder* 1965 *Hery et al* 1966 *Katsourakis and Roussas* 1966 *Spaeth* 1961) till recent publi cations by *François and his co workers* (1966 1967 1968) who proposed new etiological ideas and therapeutic possibilities

François and his co workers (1966) have demonstrated the existence of muco polysaccharides in the constitution of the lesions by means of special staining methods and histochemical analyses

Mucopolysaccharides are colored using specific staining methods and loose this coloring when the specimens are treated with hyaluronidase, acting as a

Received April th 1969

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Fig 1
Abundant fibrillary material around the islets of epitheloid cells
(Hematoxylin eosin × 25)

4 Alcian blue combined with P A S was used to show acid and neutral polysaccharides Acid mucopolysaccharides are stained in blue with Alcian blue while they become violet red with P A.S Neutral mucopolysaccharides are also stained with P A S (Fig 3)

5 Hyaluronidase digestion in Alcian blue stained sections produced a palor of the digested part (Fig 4)

6 In hyaluronidase digested sections stained with P A S and Alcian blue the P A S positive material did not disappear entirely while the blue stained acid mucopolysaccharides were completely dissolved (Fig 5)

7 P A S staining was positive and remained so after pityalin (salivary) digestion and this confirms presence of mucopolysaccharides

8 Fibrin which participates in the membrane formation was stained in blue with phospho tungistic acid hematoxylin (Fig 6)

dissolvent of hyaluronic acid and chondroitin sulphuric acid Having obtained the same results in all their work *François et al* (1966 1967 1968) forwarded the hypothesis of a disturbance of mucopolysaccarides metabolism in connective tissue and tried successfully a new treatment of ligneous conjunctivitis with local application of hyaluronidase in combination with alpha chymotrypsine

Histochemical and histopathological investigations were carried out on the biopsy material of two cases of ligneous conjunctivitis seen at the Department of Ophthalmology Hacettepe University Medical Faculty, Ankara the second been treated succesfully

Material and Method

Biopsy material was fixed in 10 % formalin and paraffin In different sections various special staining methods were used

1 Hematoxylin eosin staining for general view

2 Metochromasie with toluidine blue (Ph 3 5) for acid mucopolysaccharides (hyaluronic acid and chondroitin sulphate)

3 Alcian blue (S Gx) for acid mucopolysaccharides

4 Alcian blue and P A S for acid and neutral mucopolysaccharides

5 Sections stained with Alcian blue were digested with hyaluronidase (150 U solved in 1 cc of serum) and left in room temperature for one hour

6 Sections stained with Alcian blue and P A S were digested with hyaluronidase

7 P A S staining was also used with and without digestion

8 Phospho tungistic acid hematoxylin staining to show the fibrin content of the membrane

Results

1 Sections stained with hematoxylin eosin showed abundant inflammatory cells among membraneous tissue fine fibrilar bundles and epitheloid islets crossing each other or parallel (Fig 1)

2 A dark pink metachromatic appearence was observed in some areas with toluidine blue (Fig 2)

3 Acid mucopolysaccharides were stained by Alcian blue This dye was preferred as the Reinhardt Abul Haj colloidal technique is more complicated (*Mc Manus and Mowry*, 1960)

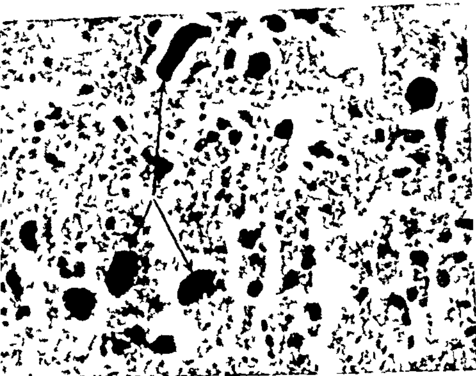


Fig ɔ

Irregular globules of Alcian blue positive material (indicated by arrows) on the back ground of P A S positive material showing acid and neutral mucopolysaccharides (Alcian blue + P A S × 63)

condition was more severe in the right eye where it was complicated by a corneal ulcer and iridocyclitis Bleeding occurred on any attempt to remove the membranes (Fig 10) Laboratory results were all negative except mucopolysaccharide dosage in the urine as the Anthrone method revealed a high level (115?/165 ml compared with normal of ?93 6/165 ml)

At this time the sensational results obtained by *François* (1967) were published and the histochemical constitution was shown (*François et al* 1966)

While carrying out histochemical investigations we started the treatment immediately We used a 1 10 000 dilution of alpha chymotrypsine and a solution of 35 U hyaluronidase per cc Two drops of these drugs were instilled in both eyes *every hour for* two months

After two weeks the hardness of the membranes was already diminished and it was easier to remove them without bleeding Seventy days after the beginning of the treatment the membranes had disappeared at the left eye and later at the right eye The keratitis healed also leaving only a paracentral nebula of the right cornea (Figs 11 1 15)

Drug dosage was gradually decreased to six drops a day and then three drops a day

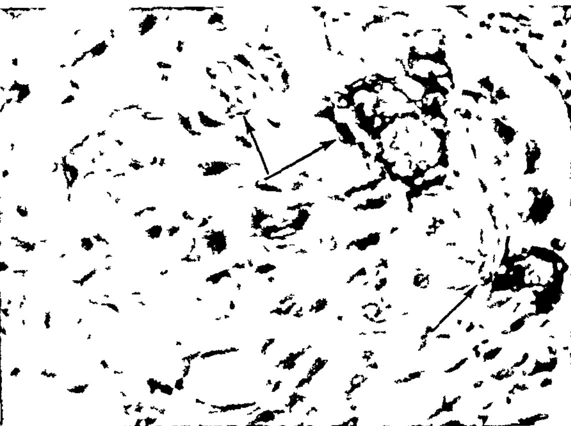


Fig 2
Metachromatic appearence indicated by arrows dark pink coloring among blue stained cells (Toluidine blue × 400)

Case Reports

Case 1 H K a 20 days old female baby showed thick white membranes on upper and lower lids of the right eye with bleeding from the conjunctiva on any attempt to remove them (Fig 7) No treatment was effective The laboratory investigations were negative Four months later the membranes were thicker and the general condition was deteriorated (raised temperature enlarged liver pharyngitis and hypochrom anemia) Group agglutinations for brucella melitensis and salmonella V D R L and Schick test were negative No microorganisms were found in the conjunctival cultures Streptococcus neisseria and pneumococcus were identified from the throat culture

Three months later the left eye was also involved in the same way (Fig 8)

Local and general antibiotics combined with steroids and local antidiphteric serum were uneffective

The child died at the age of two years from pneumonia the conjunctival membranes still present

Case 2 H A a 4 year old boy was seen in April 1968 with a typical ligneous conjunctivitis Thick membranes were found on both upper and lower lids (Fig) The

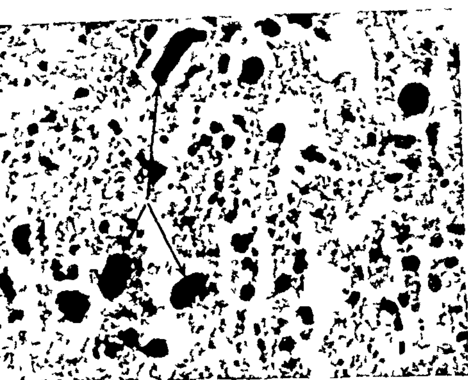


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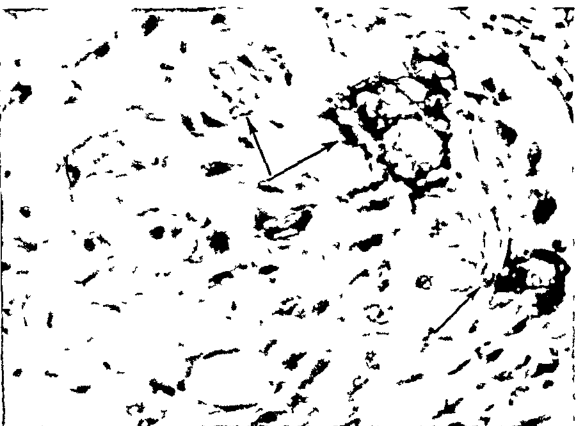


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Fig. 5

Acid mucopolysaccharides are entirely dissolved by hyaluronidase digestion while P A S material is not dissolved (arrows) (Alcian blue + P A S × [illegible])

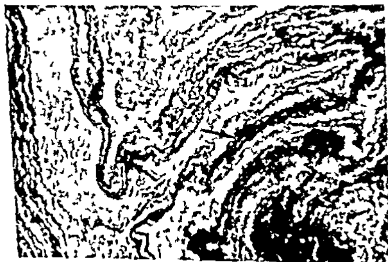


Fig 6

Wavy appearance of fine fibrine bands in the ligneous membranes (arrows) (Phosphotungistic acid + hematoxylin, × [illegible])

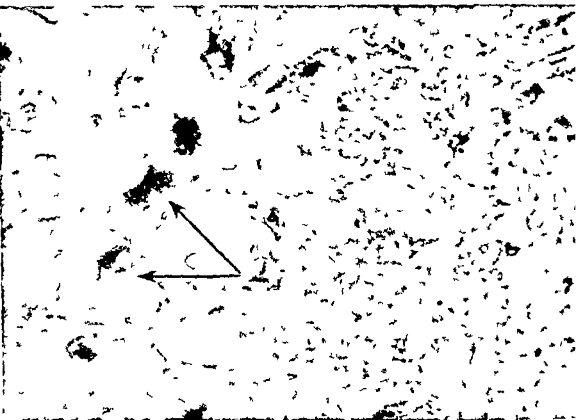


Fig 4
Section after hyaluronidase digestion The right part of the slide is pale due to digestion proving the presence of acid mucopolysaccharides while the non treated part remains darker (arrows) (Alcian blue × 400)

over a period of three and half months The patient was seen after 8 months and seemed perfectly cured

Discussion

The presence of mucopolysaccharides was shown by Alcian blue toluidine blue and P A S staining methods It was also shown that hyaluronidase dissolves acid mucopolysaccharides hyaluronic acid and chondroitin sulphate So the chemical structure of the lesions were demonstrated It was also seen that fibrin takes part in the formation of the membranes Owing to its richness in acid mucopolysaccharides the umbilical cord wos used as control material Although in some reactions there were slight differences probably due to technical

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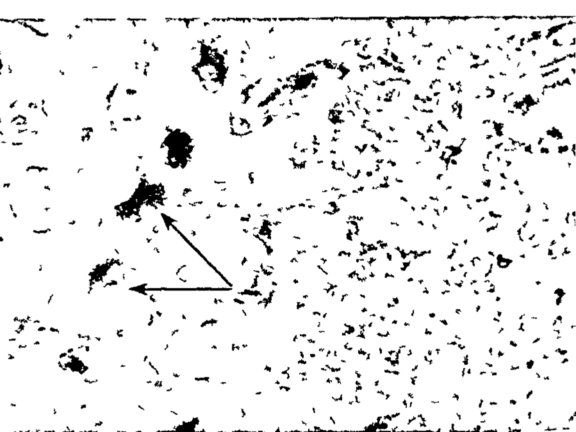


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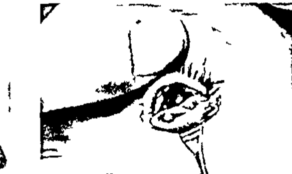


Fig 7

Case I Right eye Thick ligneoues membranes covering the tarsal conjunctiva of both lids

Fig 8

Case I Left eye Membrane formation and bleeding after attempt of removal of the membrane

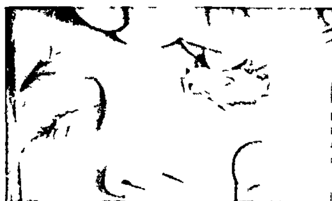


Fig 9

Case II Thick ligneoues membranes on both tarsal conjunctivas



Fig 10

Case II Bleeding of the tarsal conjunctivae after removal of the membranes

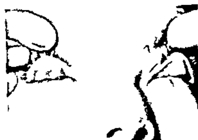


Fig 11
Case II Both upper tarsal conjunctivae looking perfectly normal after treatment



Fig 12
Case II Normal appearence of both lower tarsal conjunctivae after treatment



Fig 13
Case II Eight months after the treatment The condition is completely cured no membranes Kerato iridocyclitis healed leaving a simple scar covering 1 3 of the right lower cornea





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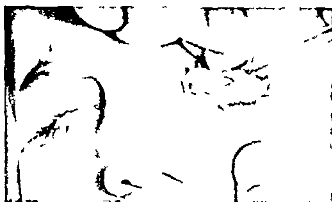


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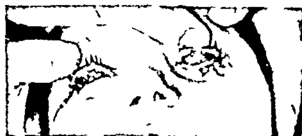


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details the special staining methods gave satisfactory results throwing light on the histochemical constitution of ligneous conjunctivitis

The treatment with hyaluronidase and alpha chymotrypsine was succesfull and gave identical results as those obtained by François His method of treat ment based on histochemical findings seems to be most effective in this rare disease the etiology and treatment of which were hitherto unknown

Summary

Histochemical and histopathological examinations were carried out on two cases of ligneous conjunctivitis observed at the Department of Ophthalmology Hacettepe University Faculty of Medicine Ankara Turkey Special staining methods demonstrated the presence of acid mucopolysaccharides confirming and emphasizing the results which François and his co warkers described for the first time in their recent publications

The second case was successfully treated by local applications of hyaluronid ase combined with alpha chymotrypsine also as advocated by François for this disease in which all previous treatments have been unsuccessfull

Acknowledgement

We are indepted to Gorenç Cılıv M D (Department of Biochemistry Hacet tepe University) who applied the Anthrone Method for the dosage of muco polysaccharides in the urine

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A FAMILY WITH BILATERAL SYMMETRICAL SECTORAL PIGMENTARY RETINAL LESION

BY

H FLEDELIUS & S E SIMONSEN

Bilateral symmetrical sectoral pigmentary lesion of the retina was first described by Bietti (3) in 1937 Since then new reports have not been numerous Thus Haase & Hellner (13) were able to collect from literature only 23 cases of sectoral pigmentary retinopathies and in some of these the fundi showed unilateral pigmentation or otherwise nonsymmetrical occurence In Scandinavia the subject has not been treated in detail before

This report deals with three patients members of the same family with symmetrical sectoral pigmentary retinal lesion Since the prognosis of the disease is not well established by follow up studies of single cases we have found it of interest to repeat examinations six years after the initial ones

Case no 1

A woman aged 59 years with hemeralopic complaints for more than 25 years There were no hereditary disorders in the family and her parents were not consanguineous Since the age of fifty she suffered from some headache and dizziness due to a benign hypertension she was therefore admitted to an ophthalmologist who discovered her retinal disorder The further investigation was performed in the Eye Clinic of Rigshospitalet

1962 Visual acuity < 6 6 in both eyes with correction Colour vision normal (Ishihara diagrams) slit lamp examination and intraocular tension normal

Perimetry a m Goldmann showed visual field defects in the upper halves (fig ?) corresponding to the affected lower retinal quadrants

Received April 18th 1969



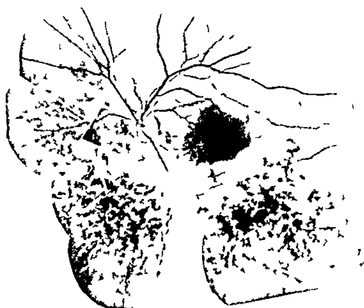


Fig 1
Fundi of patient no 1 (right eye above left eye below)

Fundi showed almost identical pictures with normal discs and macular areas and normal vessels upwards but vascular attenuation in the two lower quadrants corresponding to a demarcated semilunar yellowish area – extending from just below the discs towards the periphery – with scattered pigmentation partly of bone corpuscle type

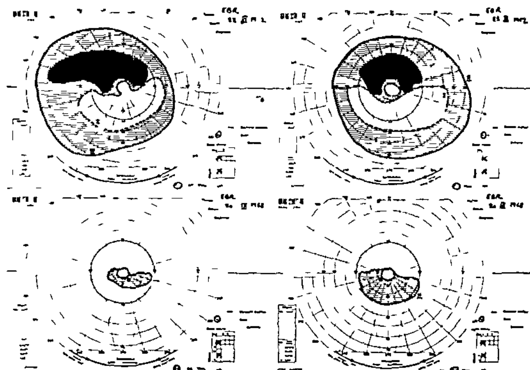


Fig 2
Visual fields of patient no 1 showing restriction from 1962 (above) to 1968 (below)

ERG a m Karpe Subnormal b waves in both eyes
X ray of cranium and sella turcica normal
WR negative
Audiometry Loss of perception for high and for low hz
Vestibular function and neurological examination normal

1968 Visual acuity 6/9 in both eyes with corr Colour vision (Ishihara) slit lamp examination and intraocular tension still normal Ophthalmoscopy showed optic discs more pale than in 1962 and some increase of the demarcated pigmented retinal areas in the lower quadrants (fig 1) Visual fields showed further restriction (fig 2)

ERG Subnormal b waves (amplitude 100 μV)

Adaptometry a m Goldmann Weeker Monophasic curve with loss of the scotopic part

Case no 2

A 38 year old healthy man without eye complaints especially no hemeralopic He is the son of patient no 1

1962 Visual acuity 6/6 in both eyes Colour vision normal (Ishihara diagrams) slit lamp examination and intraocular tension normal

His fundi showed normal discs normal macular areas and normal upper retinal quadrants but in the lower quadrants a semilunar yellowish area was seen with thin vessels and irregular pigmentations mostly pronounced in the right eye

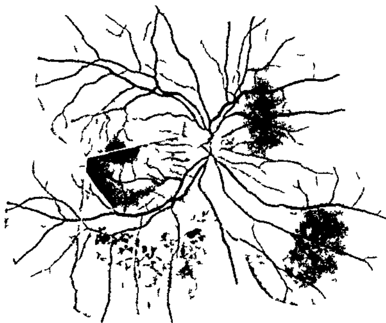




Fig 3
Fundı of patıent no 2 (rıght eye above left eye below)

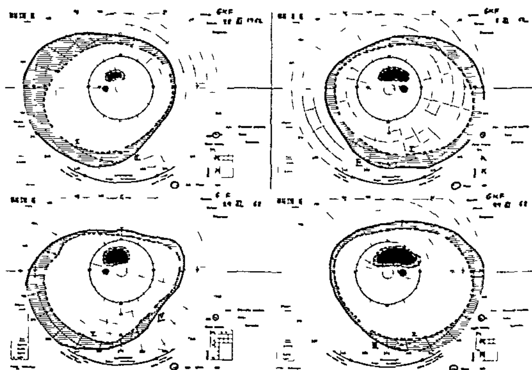


Fig 4
Visual fields of patient no 2 in 1962 (above) and 1968 (below)

Perimetry a m Goldmann showed small islet scotomas 15–20 above the point of fixation (fig 4) corresponding to the retinal lesions

ERG a m Karpe Normal b waves (amplitude 2/0 μV)

WR negative

1968 Still no eye complaints

Examinations showed results as in 1962 except increase of the affected areas and visual field defects (fig 3 4) ERG was subnormal (b wave 160 μV) in the right eye and normal (b wave 250 μV) in the less affected left eye

Adaptometry a m Goldmann-Weeker normal

Case no 3

A 61 year old man the only brother of case no 1 Apart from slight hemeralopic complaints he had no eye trouble His retinopathy was discovered in 1968

Visual acuity 6 6 in both eyes with corr

Colour vision normal (Ishihara diagrams) Slit lamp examination showed incipient cortical cataract Intraocular tension normal

Ophthalmoscopy showed normal optic discs and macular areas In the lower retinal quadrants in both eyes well demarcated yellowish areas with pigmentation very much like the fundi of case no 1

The visual field defects are shown in fig 5

ERG a m Karpe showed minimal responses (b waves 30 μV)

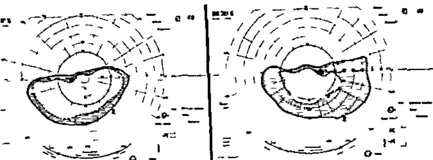


Fig 5
Visual fields of patient no 3 in 1968

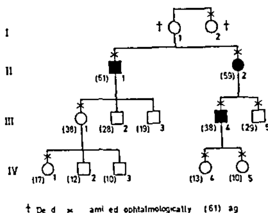


Fig 6
The family scheme Cases 1 2 and 3 are indicated with black (II 2 III4 and II 1)
Bilateral sectoral pigmentary retinopathy could not be demonstrated in the rest of the family

Discussion

Franceschetti François & Babel (9) (1963) classify the Retinopathie pigmentaire en secteur among the peripheral tapetoretinal degenerations This corresponds to Duke Elder s (1) classification of sectorial pigmentary dystrophy as a peripheral dystrophy part of the subgroup atypical pigmentary lesions

About thirty cases of bilateral symmetrical pigmentary retinopathy have been reported since Bietti s (3) original statement Several authors suggest that the disease is much more common than indicated by the number of known cases

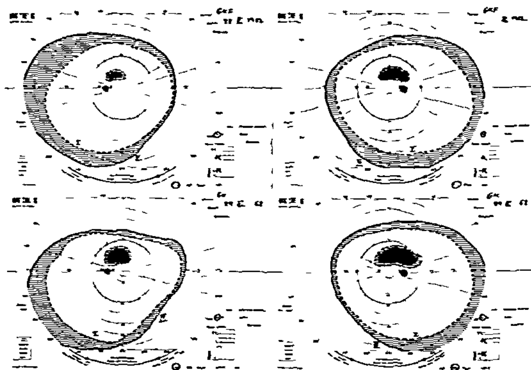


Fig 4
Visual fields of patient no 2 in 1962 (above) and 1968 (below)

Perimetry a m Goldmann showed small islet scotomas 15–20 above the point of fixation (fig 4) corresponding to the retinal lesions

ERG a m Karpe Normal b-waves (amplitude 270 μV)

WR *negative*

1968 Still no eye complaints

Examinations showed results as in 1962 except increase of the affected areas and visual field defects (fig 3 4) ERG was subnormal (b-wave 160 μV) in the right eye *and normal (b-wave 250* μV*) in the less affected left eye*

Adaptometry a m Goldmann-Weekers normal

Case no 3

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The visual field defects are shown in fig 5

ERG a m Karpe showed minimal responses (b-waves 50 μV

It is well known that defects in cochlear and vestibular function appear frequently in patients with typical retinitis pigmentosa Thus Bruno & Iolo Spada (5) examining 30 patients with typical retinitis pigmentosa found a high incidence of audiometric and also olfactory changes suggesting a causal relationship between three neuro epithelial disorders Some cases of bilateral symmetrical pigmentary lesion show defects of the auditory function too e g surdomutitas (3 24) and surditas (14) Our cases no 1 and 2 were examined otologically but no specific defects were discovered

The patients with sectoral pigmentary retinopathies are in general otherwise healthy and the disease does not regularly take part in syndromes A few exceptions do however exist Morgagni Stewart Morel syndrome in Rubino s (23) patient and Lawrence Moon Biedl syndrome in Tavolara s (26) case

The etiological problems are briefly discussed by Kuper (17) who mentions the various hypotheses The abiotrophic concept is that usually advanced A primary hereditary vascular degeneration affecting only a part of the retina has also been proposed Our fundus pictures (figs 1 and 3) seem to show some relation of the pigmentary disturbances to the retinal vascular tree It has also been emphasized that the retinal area usually affected first corresponds to the region of the fetal cleft in the eyeball but other initial retinal locations of the disorder have been reported

Summary

Three cases of hereditary bilateral symmetrical retinal pigmentary lesion are reported The disease is rare – about 30 cases are known Two of our cases have been re examined after an interval of six years both showing some progression The few symptoms and the good prognosis is however emphasized especially when compared with the typical retinitis pigmentosa

Acknowledgments

We wish to thank Dr V Ohrt for the examination of patient III 5 in the family scheme and Dr V Dreyer for the adaptometries made

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because the symptoms are too mild to make the patient consult an ophthalmologist Most cases are discovered – like ours – by accidental examination

The characteristics of the sectoral pigmentary retinal lesions can be briefly summarized The disease is usually limited to the lower retinal quadrants – preferentially the inferonasal ones – and is usually of bilateral symmetrical appearance It is said to be non progressive or very slowly progressive with only slight disturbance of dark adaptation and with good visual acuity The visual field defects usually correspond with the retinal lesions The retinal vessels are narrow only in the affected areas

ERG can be recorded the b waves show normal or subnormal values in younger and middelaged patients while they are markedly reduced in the elderly The dark adaptation curves are likewise normal in younger patients but tend to be monophasic and hemeralopic with increasing age For further details concerning ERG and adaptometry in this disease we can point out the references (6 8 10 13 14 15 17 24 28) The disease is hereditary primarily with autosomal dominant transmission (12 13 14 17 18 19) but recessive inheritance (3 24) and sexlinked transmission (9) have been reported Our family scheme (fig 6) corresponds with the dominant transmission

In comparison with the typical retinitis pigmentosa the differences are striking In the latter there is pigmentary disturbance in the whole periphery with early clinical progression leading to impaired vision ERG is abolished the adaptation curve is flattened and colour vision will be affected

In contrast to this the prognosis of the bilateral symmetrical sectoral pigmentary retinopathy is regarded as quite good – as mentioned above This is based on the observation of the extent of retinal involvement in the different age groups in families with the disorder (13 17 18 19) Thus Haase & Hellner report on three children younger than ten years with only slight pigmentary disturbances their elder sisters and brothers showed increasing involvement and the retinal lesions were pronounced in the eldest members of the family In a 73 year old woman in the family reported by Lisch (18) only tubular visual fields and a peripheral zone downwards were preserved

It is however important also to estimate the prognosis of the disease by re examinations of already known cases Klier s (16) 44 year old patient showed progression of the visual field defect by perimetry repeated after 10 weeks while Graham s (11) 28 year old patient remained absolutely unchanged during nine months Our case no 1 showed pronounced deterioration during six years subjectively as well as by ophthalmoscopy ERG and perimetry (fig 2) while case nr 2 showed only slight progression in the same period (fig 4) The small number of observations here and in other reports do not allow exact prognostic conclusions but it still seems justified to emphasize the benign clinical course with slow progression – especially as compared with the prognosis of the typical retinitis pigmentosa

From Oslo University Eye Department
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DYNAMIC TONOMETRY

II Methods of corneal indentation pulse registration

BY

IVAR HORVEN

The pulsesynchronous changes in eye tension may be studied in detail by use of the dynamic tonometer which is an improved Schiøtz electronic tonometer (*Hørven* 1968) In its present state this instrument yields an output of one mV per μ plunger deflection as shown in Fig 1 As suggested by *Bron et al* (1967) the recorded pulsations in eye tension may be regarded as an indentation pulse The difference between the highest and lowest points on each wave gives the amplitude of the indentation pulse which is recorded in mV and converted into microns of plunger deflection As known the Schiøtz weight tonometer yields a plunger deflection of 50 μ between each scale reading

The purpose of the present paper is to study in which manner the various tonometry parameters V P P_t and ΔV may be applied to the microns of indentation pulse amplitudes at various eye tension levels

V_c

Friedenwald (1957) presented in his table IV the volume of corneal indentation (V) in mm³ at half a scale reading (R) intervals This offers the opportunity to calculate the volume of corneal indentation which corresponds to one μ plun

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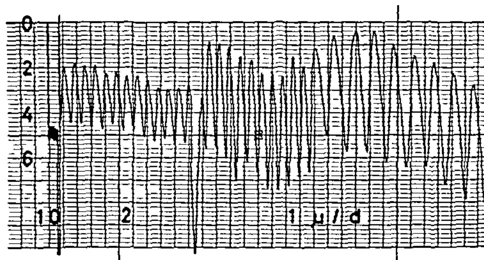


Fig 1

Normal indentation pulse of 2 µ amplitude recorded at eye tension R = 5 with the *sensitivity settings 10 2 and 1 mV per paper division One mV equals 1 µ plunger* deflection Paper speed 1 5 and 10 mm per second

ger deflection (ΔV_c) at different eye tension levels The calculation of $\Delta V_{c,}$ *is performed in the following manner at R = 0* and *R = 13* measured with the 5 5 g plunger weight

$$\Delta V_{c\,(0)} = \frac{V_{c(0\,5)} - V_{c(0)}}{25} = \frac{4\,96 - 4\,38}{25} = 0\,0232\ mm^3/\mu$$

$$\Delta V_{,(13)} = \frac{V_{c(13\,5)} - V_{c(13)}}{25} = \frac{33\,43 - 31\,87}{25} = 0\,0624\ mm^3/\mu$$

The calculated $\Delta V_{c,}$ values at R = 0 and *R = 13 are actually the mean $\Delta V_{c,}$* values of R = 0–0 5 and R = 13–13 5 No correction of this fact seems how ever necessary When performing dynamic tonometry the eye tension is first recorded followed by indentation pulse amplitude registrations As known the intraocular pressure demonstrates a moderate decrease during the period the tonometer is resting on the eye Accordingly the indentation pulse is actually recorded at eye tension R = 0 0 5 and R = 13 13 5 The above easy way of $\Delta V_{c,}$ calculation seems therefore appropriate for practical use As demon strated $\Delta V_{c,}$ in mm³/µ increases with increasing values of R An excellent li near correlationship is demonstrated between the ΔV_c values in mm³/µ plotted versus R as shown in Fig 2 The correlationship between $\Delta V_{c,}$ and R may therefore be expressed through the equation $\Delta V_c = a + b\ R$ The numerical values of a and b have been calculated for the various plunger weights and the

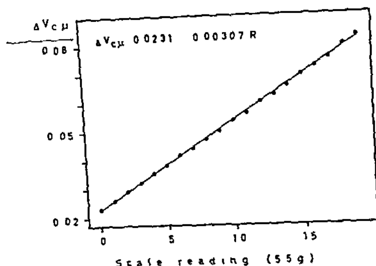


Fig 2

Corneal indentation volume (ΔV_c) in mm³ per μ plunger deflection plotted versus scale readings

actual correlation between the calculated $\Delta V_{c\mu}$ values and the straight line is given by the correlation coefficient r

(1) $\Delta V = 0\,0231 + 0\,00307$ R (5 5 g r = 0 9996)
(2) $\Delta V = 0\,0188 + 0\,00336$ R (7 5 g r = 0 9994)
(3) $\Delta V = 0\,0149 + 0\,00345$ R (10 g r = 0 9987)

Example The change in corneal indentation volume (ΔV_c) which corresponds to an indentation pulse of 30 μ amplitude recorded at R = 5 with the 5 5 g plunger weight is calculated as follows

$$\Delta V = 30 \quad \Delta V_c = 30(0\,0231 + 0\,00307 \quad 5) = 1\,15 \text{ mm}^3$$

The V values of Friedenwald were calculated by use of the equation

$$(4) \log P_t = B - \frac{1}{0\,016} \log V_c$$

In order to obtain an estimate of B the V value at R = 5 was calculated by use of the formula log P = log P_t - k V. A P value of 17 3 mm Hg and the average normal ocular rigidity coefficient value of 0 0215 were used these values had previously been determined by Friedenwald The factor B could then be estimated by insertion of this calculated V value in equation (4) Friedenwald s procedure of V calculation by equation (4) depends therefore not

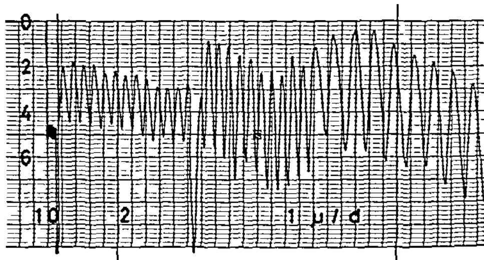


Fig 1

Normal indentation pulse of 2, μ amplitude recorded at eye tension R = 5 with the sensitivity settings 10 2 and 1 mV per paper division One mV equals 1 μ plunger deflection Paper speed 1 5 and 10 mm per second

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As demonstrated in Fig 3 (top) the ΔP_0 values increase markedly with increasing intraocular pressure i e with decrease in R An excellent linear correlationship is demonstrated (Fig 3 bottom) when the various log ΔP_0 values are plotted versus R fitting the equation log ΔP_0 = a + b R – 2 The values of a and b have been calculated for the various plunger weights as follows

(8) log ΔP_0 = 1 1328 – 0 0738 R – 2 (5 5 g r = 0 9995)

(9) log ΔP_0 = 1 2671 – 0 0694 R – 2 (7 5 g r = 0 9995)

(10) log ΔP = 1 3874 – 0 0660 R – 2 (10 g r = 0 9995)

Example The ΔP_0 value which corresponds to an indentation pulse of 30 μ amplitude recorded at R = 5 with the 5 5 g plunger weight is calculated as follows

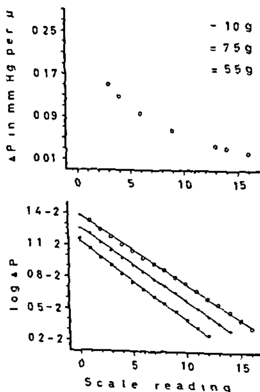


Fig 3

Changes in intraocular pressure (ΔP) in mm Hg per u plunger deflection at various scale readings (top) Log ΔP_{μ} plotted versus scale readings demonstration of excellent linear correlat onship at all plunger weights (bottom)

only on the validity of his P_t values but also on the rigidity coefficient value of 0 0215 As demonstrated by *Ytteborg* (1960), *Eisenlohr et al* (1962) *Hetland Eriksen* (1966) and others Friedenwald s rigidity coefficient value of 0 0215 is probably too large

By use of an experimental set up on freshly enucleated human eyes Hetland Eriksen measured the volume of displaced fluid which occurred by mechanical Schiøtz tonometry (V_t) and found higher values than reported by Friedenwald Hetland Eriksen s data permits calculation of the volume of displaced fluid in mm³ which corresponds to one μ plunger deflection ($\Delta V_{t\mu}$) at various eye tension levels A fair linear correlationship is demonstrated when the $\Delta V_{t\mu}$ values are plotted versus R which offers the opportunity of presenting the Hetland Eriksen data by the following equations

(5) $\Delta V_{t\mu} = 0\ 0269 + 0\ 00317 \quad R \quad (5\ 5\ g \quad r = 0\ 9846)$
(6) $\Delta V_{t} = 0\ 0247 + 0\ 00271 \quad R \quad (7\ 5\ g \quad r = 0\ 9851)$
(7) $\Delta V_{t\mu} = 0\ 0208 + 0\ 00282 \quad R \quad (10\ g \quad r = 0\ 9950)$

Example The volume of displaced fluid (ΔV_t) which corresponds to an indentation pulse of 30 μ amplitude recorded at R = 5 with the 5 5 g plunger weight will be

$$\Delta V_t = 30 \quad \Delta V_{t\mu} = 30(0\ 0269 + 0\ 00317 \quad 5) = 1\ 28\ \text{mm}^3$$

Accordingly the results obtained by use of Hetland Eriksen s data yield roughly 10 % larger values than the results obtained by use of Friedenwald s data

P_o

Friedenwald calculated the intraocular pressure before tonometry (P_o) by use of the formula $\log P_o = \log P_t - K \quad V_c$ where K is the ocular rigidity coefficient of 0 0215 As mentioned above Friedenwald s V_c values are probably too small and his rigidity coefficient value of 0 0215 probably too large These discrepancies will however to some extent work against each other in the product K V_c His P_o values are therefore accepted for practical use without further reservations

The change in intraocular pressure before tonometry which corresponds to a plunger deflection of one μ ($\Delta P_{o\mu}$) is calculated at R = 2 with the 5 5 g plunger weight as follows

$$\Delta P_{o\mu(\ )} = \frac{P_{o(2)} - P_{o(\ )}}{25} = \frac{28\ 97 - 26\ 56}{25} = 0\ 0964\ \text{mm Hg}/\mu$$

In this manner the various $\Delta P_{o\mu}$ values may be calculated at all tension levels

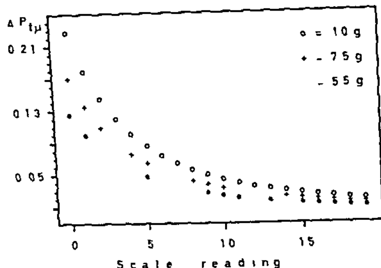


Fig 4

Changes in intraocular pressure (ΔP_t) in mm Hg per μ plunger deflection at various scale readings

pressure as shown in Fig 4 A linear correlationship was not demonstrated neither between ΔP_t plotted versus R nor between log ΔP_t plotted versus R The ΔP_t values are therefore given in mm Hg per μ plunger deflection at the various eye tension levels and with the three plunger weights in Table II

ΔV

Friedenwald calculated the change in ocular volume (ΔV) for various plunger weights when the tonometer reading falls from 0 to R by use of the equation

$$(11) \quad \Delta V = \frac{1}{K} \log \frac{P_t}{P_{tR}} + V_R - V$$

A fair linear correlationship is demonstrated when plotting the ΔV values versus R as shown in Fig 5 The ΔV points are not however distributed at random around this straight line but yields a definite upward concave slope suggesting that the data would better fit into the equation $y = a + bx + cx$ In Fig 6 this equation has been used with $x = 0$ at $R = 8$ 5 An excellent correlation is noted For a practical purpose therefore ΔV may be calculated directly from R with a fair degree of accuracy by use of this equation with the following values for a b and c for various plunger weights

$$\log \Delta P_t = 1.1328 - 0.0738 \cdot 5 - 2 = 0.7638 - 2$$

$$\Delta P_{o/} = 0.058 \text{ mm Hg}/\mu$$

$$\Delta P_o = 30 \cdot \Delta P_o = 30 \cdot 0.058 = 1.74 \text{ mm Hg}$$

Table I offers the ΔP_o values in mm Hg per μ plunger deflection which may be calculated by use of equations (8) (9) (10) for various scale readings and plunger weights

P_t

The change in intraocular pressure during tonometry which corresponds to a plunger deflection of one μ ($\Delta P_{t/}$) may be calculated by use of Friedenwald's P_t data at the various eye tension levels in an identical manner as for $\Delta P_{o/}$. The $\Delta P_{t/\!/}$ values demonstrate a marked increase with increasing intraocular

Table I

ΔP_t in mm Hg per μ plunger deflection

R	5.5 g	7.5 g	10 g	R	5.5 g	7.5 g	10 g
0	0.1358	0.1850	0.2440	10	0.0248	0.0374	0.0534
0.5	0.1258	0.1708	0.2261	10.5	0.0228	0.0345	0.0495
1	0.1146	0.1577	0.2096	11	0.0209	0.0319	0.0459
1.5	0.1052	0.1455	0.1943	11.5	0.0192	0.0294	0.0425
2	0.0967	0.1344	0.1801	12	0.0177	0.0272	0.0394
2.5	0.0888	0.1241	0.1669	12.5	0.0162	0.0251	0.0365
3	0.0816	0.1145	0.1546	13	0.0149	0.0232	0.0338
3.5	0.0749	0.1057	0.1433	13.5	0.0137	0.0214	0.0314
4	0.0688	0.0976	0.1328	14	0.0126	0.0197	0.0291
4.5	0.0632	0.0901	0.1231	14.5	0.0116	0.0182	0.0270
5	0.0580	0.0832	0.1141	15	0.0106	0.0168	0.0250
5.5	0.0533	0.0768	0.1058	15.5	0.0097	0.0155	0.0231
6	0.0490	0.0708	0.0980	16	0.0090	0.0143	0.0215
6.5	0.0450	0.0655	0.0908	16.5	0.0082	0.0132	0.0199
7	0.0413	0.0604	0.0842	17	0.0076	0.0122	0.0184
7.5	0.0380	0.0558	0.0780	17.5	0.0069	0.0113	0.0171
8	0.0349	0.0151	0.0724	18	0.0064	0.0104	0.0158
8.5	0.0320	0.0476	0.0671	18.5	0.0059	0.0096	0.0147
9	0.0294	0.0439	0.0622	19	0.0054	0.0089	0.0136
9.5	0.0270	0.0405	0.0576	19.5	0.0049	0.0082	0.0126

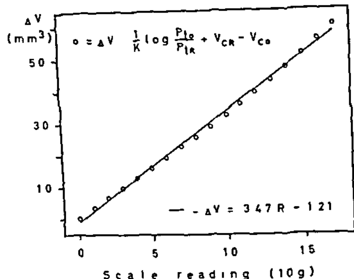


Fig 5

Changes in ocular volume (ΔV) in mm³ when the plunger moves from 0 to R plotted versus scale readings a fair linear correlationship is noted

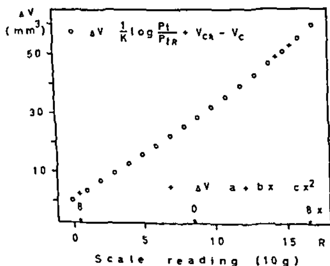


Fig 6

Changes in ocular volume (ΔV) in mm when the plunger moves from 0 to R as given by Friedenwald (o) Theoretically calculated ΔV values fitting the equation

$y = a + b \quad x + c \quad x^2$ (+)

Table II

ΔP_{t_0} in mm Hg per μ plunger deflection

R	5.5 g	7.5 g	10 g	R	5.5 g	7.5 g	10 g
0	0.1244	0.1696	0.2264	10	0.0248	0.0336	0.0448
0.5	0.1104	0.1504	0.2008	10.5	0.0232	0.0316	0.0424
1	0.0984	0.1344	0.1788	11	0.0220	0.0300	0.0400
1.5	0.0884	0.1204	0.1608	11.5	0.0208	0.0288	0.0384
2	0.0796	0.1088	0.1448	12	0.0200	0.0272	0.0360
2.5	0.0724	0.0984	0.1312	12.5	0.0192	0.0256	0.0344
3	0.0656	0.0900	0.1200	13	0.0180	0.0248	0.0332
3.5	0.0604	0.0820	0.1096	13.5	0.0172	0.0236	0.0312
4	0.0552	0.0756	0.1004	14	0.0164	0.0224	0.0300
4.5	0.0512	0.0696	0.0928	14.5	0.0156	0.0212	0.0284
5	0.0472	0.0640	0.0860	15	0.0152	0.0208	0.0276
5.5	*0.0436*	*0.0596*	*0.0792*	*15.5*	*0.0144*	0.0196	*0.0260*
6	0.0408	0.0556	0.0740	16	0.0140	0.0188	0.0252
6.5	0.0380	0.0516	0.0688	16.5	0.0132	0.0180	0.0244
7	0.0352	0.0484	0.0644	17	0.0128	0.0176	0.0232
7.5	0.0332	0.0452	0.0604	17.5	0.0120	0.0168	0.0220
8	0.0312	0.0424	0.0568	18	0.0120	0.0160	0.0216
8.5	0.0292	0.0400	0.0532	18.5	0.0112	0.0156	0.0204
9	0.0276	0.0376	0.0500	19	0.0112	0.0148	0.0200
9.5	0.0260	0.0356	0.0472	19.5	0.0104	0.0144	0.0192

(12) $\Delta V = 22.8758 + 3.5945 \cdot x + 0.0204 \cdot x^2$ (5.5 g x = R−6.5)
(13) $\Delta V = 25.1675 + 3.5370 \cdot x + 0.0344 \cdot x^2$ (7.5 g x = R−7.5)
(14) $\Delta V = 27.2198 + 3.4587 \cdot x + 0.0409 \cdot x^2$ (10 g x = R−8.5)

Example ΔV at R = 5 respective R = 10 with the 5.5 g plunger weight is calculated as follows

$x = R - 6.5 = 5 - 6.5 = -1.5$
$\Delta V = 22.8758 + 3.5945 \cdot (-1.5) + 0.0204 \cdot (-1.5)^2 = 17.53 \text{ mm}^3$
$x = R - 6.5 = 10 - 6.5 = 3.5$
$\Delta V = 22.8758 + 3.5945 \cdot 3.5 + 0.0204 \cdot 3.5^2 = 35.71 \text{ mm}^3$

It is stressed that even if the correlation between the equation $y = a + bx + cx^2$ and Friedenwald's ΔV data is excellent the two curves are not identical and a minor discrepancy between their various decimal values should be expected. In the following therefore Friedenwald's original data as listed in his Table VII are used for calculation of $\Delta V/\mu$ i.e. the change in ocular volume which yields a plunger deflection of one μ at various eye tension levels. The

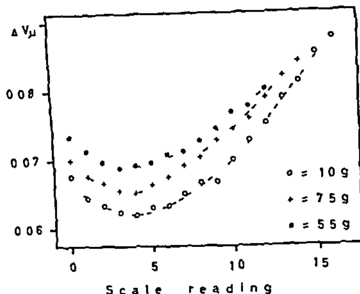


Fig 7
Change in ocular volume in mm³ per μ plunger deflection (ΔV_μ) calculated from Friedenwald s data at various scale readings

If $R = 0 5 + R_1$ equation (15) may be used to calculate the various ΔV differences at all tension levels Dividing the results by 25 gives the various ΔV_μ values in mm³ per μ plunger deflection

As suggested by Friedenwald the pressure volume relationship of the eye may be expressed by the equation

$$K \quad \Delta V = \log P - \log P_1 \text{ which gives } \Delta V = \frac{1}{K} \log \frac{P}{P_1}$$

In equation (15) the first part of the formula

$\left(\frac{1}{K} \log \frac{P_R}{P_{tR}}\right)$ will therefore indicate a change in volume

$$(16) \quad \Delta V = \frac{1}{K} \log \frac{P}{P_1} \text{ if } P = P_{tR} \text{ and } P_1 = P_{tR}$$

The latter part of equation (15) ($V_R - V_R$) indicates a change in corneal indentation of $\Delta V_{(R_1-R)}$ Equation (15) may therefore be expressed as

$$(17) \quad \Delta V_{(R_1-R)} = \Delta V + \Delta V$$

From this equation (17) it is obvious that the change in ocular volume $\Delta V_{(R_1-R)}$

method employed for these calculations is identical with the one described above for calculation of the various ΔV_e values The results obtained are listed in Table III and demonstrated in Fig 7 An increase in ΔV_r values exists at lower intraocular pressures which was to be expected because of the previously mentioned upward concave slope of the ΔV curve (Fig 6) The increase in ΔV_a which occurs at R = 0 3 may however need some explanation By use of equation (11) ΔV may be calculated for various values of R Calculating ΔV for R_1 and R the difference will be

$$\Delta V_{R_2} - \Delta V_{R_1} = \frac{1}{K} \log \frac{P_{t_2}}{P_{tR}} + V_{cR_2} - V_{co}$$

$$- \left(\frac{1}{K} \log \frac{P_{to}}{P_{tR}} + V_{cR} - V_{co} \right)$$

$$(15) \quad \Delta V_{(R_2-R)} = \frac{1}{K} \log \frac{P_{tR}}{P_R} + V_{cR} - V_{cR}$$

Table III

Changes in ocular volume in mm per μ plunger deflection (ΔV_r)

R	(Friedenwald) 5 5 g	7 5 g	10 g	R	(Langham and Hetland Eriksen) 5 5 g	7 5 g	10 g
0	0 0736	0 0700	0 0676	0	0 1570	0 1550	0 1510
1	0 0712	0 0676	0 0644	1	0 1370	0 1345	0 1305
2	0 0696	0 0668	0 0632	2	0 1225	0 1195	0 1155
3	0 0688	0 0656	0 0624	3	0 1130	0 1095	0 1055
4	0 0692	0 0652	0 0620	4	0 1050	0 1010	0 0970
5	0 0696	0 0664	0 0632	5	0 1000	0 0955	0 0920
6	0 0708	0 0676	0 0636	6	0 0970	0 0920	0 0885
7	0 0712	0 0692	0 0652	7	0 0950	0 0900	0 0865
8	0 0728	0 0704	0 0668	8	0 0950	0 0890	0 0860
9	0 0744	0 0728	0 0688	9	0 0955	0 0890	0 0860
10	0 0768	0 0744	0 0700	10	0 0970	0 0900	0 0875
11	0 0776	0 0760	0 0728	11	0 0980	0 0910	0 0880
12	0 0800	0 0788	0 0752	12	0 0990	0 0915	0 0885
13	0 0819	0 0820	0 0788	13	0 1000	0 0920	0 0890
14	0 0832	0 0840	0 0812	14	0 1020	0 0930	0 0905
15	0 0870	0 0872	0 0852	15	0 1035	0 0945	0 0920
16	0 0895	0 0892	0 0872	16	0 1050	0 0955	0 0930
17	0 0909	0 0932	0 0900	17	0 1070	0 0970	0 0945
18	0 0950	0 0964	0 0943	18	0 1080	0 0975	0 0955
19	0 0980	0 0976	0 0974	19	0 1090	0 0980	0 0960

$$\Delta V_{(R \to R)} = \frac{1}{K} \log \frac{\frac{W}{a + b \ R_1}}{\frac{W}{a + b \ R}} + V_R - V_{eR}$$

$$= \frac{1}{K} \log \frac{a + b \ R}{a + b \ R_1} + \Delta V_{(R \to R)}$$

The first part of this equation ($\frac{1}{K} \log \frac{a + b \ R}{a + b \ R_1}$) reflects ΔV_e which accordingly is dependent upon variations in R and K alone not in plunger weights

As mentioned above Friedenwald s average normal rigidity coefficient va lue of 0 0215 is probably too large Experimental studies by *Langham* (1963) concerning the pressure volume relationship of the eye yields lower rigidity coefficient values in addition to support the view that the rigidity coefficient demonstrates a significant decrease with increasing intraocular pressure These findings are confirmed by the experimental data offered by *Ytteborg* (1960) and *Hetland Eriksen* (1966) As the P_t values of Friedenwald were based on experimental data and not calculated by use of his rigidity coefficient value of 0 0215 his P_t values are of the same order of magnitude as found by other authors and may be trusted for clinical use The change in ocular volume (ΔV_e) may accordingly be calculated from Langham s data corresponding to the va rious levels of intraocular pressure offered by Friedenwald s P_t table for each scale reading This has been done in Fig 9 A large difference is noted between the ΔV_e values calculated by use of Langham s data compared with the ΔV_e values calculated through equation (16) by use of Friedenwald s data

In Fig 10 the ΔV_e values of Langham is added to the ΔV_t values of Het land Eriksen (top) and the $\Delta V_{c\mu}$ values of Friedenwald (bottom) The ΔV_μ va lues of Langham – Hetland Eriksen are somewhat larger than Langham – Frie denwald s values because of the previously discussed difference in their ΔV respective ΔV_t values More important the ΔV_μ values of Langham – Hetland Eriksen which are based on equations (5) (6) (7) and listed in Table III are significantly and strikingly larger than the ΔV values based on Friedenwald s data as shown in Fig 8 and Table III

In spite of the convenience of using Friedenwald s 1955 tables it seems at present more reasonable to use data which may be confirmed by experimental procedures on human eyes This is certainly most important when dealing with the ΔV values because of the large difference which exists between Frieden wald s theoretically based figures compared with Langham and Hetland Erik sen s experimentally ones According to authors opinion therefore the Lang ham – Hetland Eriksen data should be preferred in the procedure of converting the indentation pulse amplitude in μ plunger deflection into a corresponding

which occurs during tonometry when the plunger moves from R_1 to R_2 is actually composed of two different volumes ΔV_e and ΔV_c. The ΔV_e will reflect the change in ocular volume which corresponds to the difference in intraocular pressure at eye tension level R_1 and R_2, whereas the ΔV_c will reflect the change in corneal indentation which occurs by a plunger displacement from scale reading R_1 to R_2. If $R_2 = 0.5 + R_1$ and the various volume differences are divided by 25, the ΔV_μ, $\Delta V_{e\mu}$ and $\Delta V_{c\mu}$ values are obtained as previously described. This is visualized in Fig. 8. At high intraocular pressures (R = 0-3) the $\Delta V_{e\mu}$ values are large, which explains the increase in ΔV_μ values demonstrated above (*Fig. 7*).

It has previously been demonstrated that the ΔV_e and $\Delta V_{t\mu}$ values change with different plunger weights (equations (1) (2) (3) and (5) (6) (7)). The ΔV_c values are not, however, dependent upon plunger weights. This may be visualized by use of Friedenwald's formula for P_t calculation: $\frac{W}{P_t} = a + b \cdot R$, i.e. $P_t = \frac{W}{a + b \cdot R}$, where W is the weight of the plunger assembly and a and b are constants used at all plunger weights without change of their numerical values. Inserting $\frac{W}{a + b \cdot R}$ in equation (15) gives

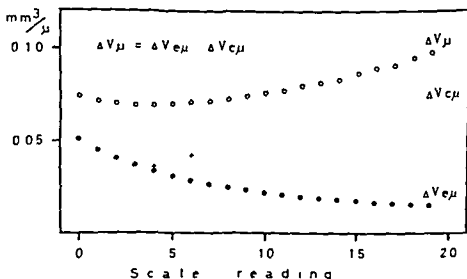


Fig. 8

The change in ocular volume in mm³ per μ plunger deflection (ΔV_μ) consists of two parameters ΔV_e and ΔV_c. The first is most important at higher levels, the latter is most important at lower levels of intraocular pressure (Friedenwald's data)

$$\Delta V_{(R_1-R)} = \frac{1}{K} \log \frac{\dfrac{W}{a + b\ R_1}}{\dfrac{W}{a + b\ R}} + V_R\ - V_R$$

$$= \frac{1}{K} \log \frac{a + b\ R_2}{a + b\ R_1} + \Delta V\ _{(R_1-R)}$$

The first part of this equation ($\frac{1}{K}$ log $\frac{a + b\ R_2}{a + b\ R_1}$) reflects ΔV_e which accordingly is dependent upon variations in R and K alone not in plunger weights

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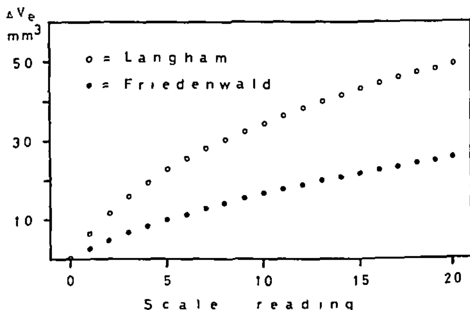


Fig 9

The change in ocular volume (ΔV_e) which occurs when the intraocular pressure falls from 51 4 mm Hg ($P_{tR=0}$) to 14 4 mm Hg ($P_{tR=\infty 0}$) Please note the striking difference between Langham s (o) and Friedenwald s ( ) data

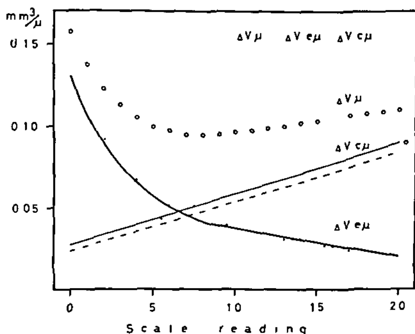


Fig 10

The change in ocular volume in mm³ per μ plunger deflection (ΔV_μ) which is formed by adding Langham s $\Delta V_{e\prime}$ data to Hetland Eriksen s $\Delta V_{t\prime}$ data (o) and to Friedenwald s ΔV_c data (+) (5 5 g plunger weight)

change in ocular volume This may be visualized by the following example An indentation pulse of 30 μ amplitude recorded with the 5 5 g plunger weight at R = 2 and R = 8 will correspond to the following changes in ocular volume

	Friedenwald	Langham – Hetland Eriksen
R = 2	2 088 mm³	3 675 mm³
R = 8	2 184 mm³	2 850 mm³

Comment

A corneal indentation pulse of a certain amplitude in μ may be converted into mm Hg P values mm Hg P_t values mm³ of corneal indentation or mm³ change in ocular volume as described above The advantage of converting the μ indentation pulse value into one or all of these parameters is stressed by the fact that a certain μ indentation pulse amplitude yields different values of these parameters depending on the eye tension level As the indentation pulse primarily reflects the change in ocular volume produced by the excess of blood entering the eye at each pulse beat the most appropriate and practical method of indentation pulse registration should be to convert the μ amplitude into a corresponding change in ocular volume in mm³ by use of Table III By doing so it should also be stated whether Friedenwald s or the preferable Langham – Hetland Eriksen s data are used for this conversion as these two pairs of converting tables differ markedly from each other



Summary

The corneal indentation pulse recorded in μ plunger deflection by use of dynamic tonometry reflects changes in the tonometry parameters P_o P_t V_c and ΔV The present paper supplies formulas and converting tables which should facilitate the procedure of converting the indentation pulse amplitude in μ plunger deflection into one or all of these parameters at all tension levels

Acknowledgment

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Rikshospitalet Oslo Norway
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DYNAMIC TONOMETRY

III The corneal indentation pulse in normal and glaucomatous eyes

BY

IVAR HØRVEN

The corneal indentation pulse has previously been recorded by use of various methods An electronic tonometer of conventional type was employed by *Dastanger* (1963) and *Bron et al* (1967) *Bynke & Krakau* (1964) approached the problem by development of a new technique for corneal indentation pulse registration called oculosphygmography This technique mav be handy for clinical comparison of the indentation pulse in the two eyes of the same subject It suffers the disadvantage however of not offering the possibility of convertion of the recorded pulsations into change in mm Hg intraocular pressure or mm³ ocular volume This difficulty may be overcome by use of the dynamic tonometer which is an improved standardized Schiøtz electronic tonometer supplied with a zero suppression unit (*Hørven* 1968 a) and for which the necessary convertion tables have been provided (*Hørven* 1970)

The corneal indentation pulse registration may be of diagnostic interest in various diseases which in one way or another affect the ocular blood supply Thus a decrease of the indentation pulse have been demonstrated in carotid artery occlusive disease (*Castren & Lavikainen* 1964 *Bynke & Krakau* 1964 *Bynke* 1966 *Bron et al* 1967 *Galin* 1967) following optic glioma resection (*Bynke & Krakau* 1964 *Hørven* 1968 b) and in giant cell arteritis (*Hørven* 1968 c) A decrease in ocular pulsation have also been demonstrated in luetic

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choroidal atrophy (*Suzuki* 1962) and tapetoretinal degeneration (*Horven* 1968b) An increase of the indentation pulse amplitude may be present in eyes harboring choroidal melanomas (*Horven* 1969 a) during pain attacks of cluster headache (*Broch et al* 1970) in carotid cavernous fistula (*Boyes & Ralph* 1954 *Horven* 1968 b) and Sturge Weber s disease (*Flage & Horven* 1970)

The known pressure volume relationship of the eye implies that if the increase in ocular blood volume in systole is the same with high as with low intraocular pressure the pulsations in ocular pressure will be greatest when the pressure is high", a formulation offered by *Davanger* (1964) In his studies on ocular pulsation *Davanger* (1963) found that the pulsesynchronous changes in intraocular pressure increased with increasing pressure levels The corresponding indentation pulse amplitude and the mm³ change in ocular volume were however fairly constant at all eye tension levels *Comberg & Pilz* (1961) measured enlarged indentation pulse amplitudes in eyes with elevated intraocular pressure providing that the pressure elevation was produced by an increase of the venous pressure obtained by insufflation of a neck cuff If the intraocular pressure was elevated by manual compression of the eye ball no enlargement of amplitudes was found *Bynke* (1968) on the other hand demonstrated increase of indentation pulse amplitudes by elevated intraocular pressure levels findings which suggest that an increase also exists in mm³ change in ocular volume

This problem will be delt with in the present study which main purpose is to evaluate the normal values of corneal indentation pulse amplitudes at various levels of intraocular pressure in normal and glaucomatous eyes

Material

The present study includes observations in 150 patients with a total of 205 eyes The material is composed as follows

Eyes with normal intraocular pressure i e with eye tension between Schiøtz scale reading 3 5 and 10 measured with the 5 5 g plunger weight

A 100 normal eyes from 100 patients Age 5 81 years Sex 61 females 39 males

B 27 glaucomatous eyes from 27 glaucoma patients Age 40 80 years Sex 17 females 10 males These eyes were all under adequate treatment for glaucoma a surgical procedure had previously been performed in some of them

C 65 mate eyes from the above (A) 100 patients These eyes were either normal or suffered from eye diseases which to our present state of knowledge do not affect the size of the indentation pulse amplitude

D 13 mate eyes from the above (B) 27 glaucoma patients These eyes were also under adequate treatment for glaucoma

Eyes with pathologically increased intraocular pressure i e with eye tension between scale reading -1 and 3 measured with the 5 5 g plunger weight

E 45 glaucomatous eyes from 23 glaucoma patients All of these eyes were under heavy but inadequate medical treatment for their glaucoma

Methods

Dynamic tonometry was performed with the 5 5 g plunger weight Following eye tension registration the indentation pulse was recorded with a sensitivity setting of 2 and 1 mV per paper division 1 mV output equals one μ plunger deflection The indentation pulse amplitude in μ plunger deflection was converted into mm³ change in ocular volume (ΔV) by use of the Langham – Hetland Eriksen data and the pulsesynchronous change in mm Hg intraocular pressure (ΔP ΔP_t) were calculated as previously described (*Horven* 1970)

Dynamic tonometry is performed on patients in the supine position just like an ordinary Schiotz tonometry It is of major importance however to keep the tonometer head in the exact vertical position with the plunger resting on the very center of the cornea To avoid sticking of the plunger frequent cleaning is necessary This is especially true when dynamic tonometry is performed on very soft eyes which yield rather small indentation pulse amplitudes

Results

The results obtained by dynamic tonometry examinations are listed in Table I In the 100 normal eyes (A) a mean corneal indentation pulse amplitude of 30 02 μ (σ = 10 048) was obtained Identical values were found in all the other normotensive eye groups (B C D) When all these groups are pooled together (A + B + C + D) a mean indentation pulse amplitude of 29 84 μ (σ = 9 610) is obtained The 45 hypertensive glaucoma eyes (E) yielded a mean indentation pulse value of 43 09 μ (σ = 17 666) When these hypertensive glaucoma eyes (E) are tested statistically by application of the Students t test against the normotensive glaucoma eyes (B + D) and against the total number of normotensive eyes (A + B + C + D) a t value of 4 388 respective 4 876 was obtained The difference in corneal indentation pulse amplitudes demonstrated between the hypertensive and normotensive eye groups is therefore considered as highly significant (P < 0 001)

In order to study in detail the relationship between corneal indentation pulse amplitudes and intraocular pressure the values obtained at various eye tension

choroidal atrophy (*Suzuki* 1962) and tapetoretinal degeneration (*Horven* 1968b) An increase of the indentation pulse amplitude may be present in eyes harboring choroidal melanomas (*Horven* 1969 a) during pain attacks of cluster headache (*Broch et al* 1970) in carotid cavernous fistula (*Boyes & Ralph* 1954 *Horven* 1968 b) and Sturge Weber s disease (*Flage & Horven* 1970)

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levels are listed with half a scale reading intervals in Table II and visualized in Fig 1 Fig 1 demonstrates that the increase in μ indentation pulse amplitudes at higher levels of intraocular pressure is comparatively smaller than the corresponding increase in mm³ (ΔV) and mm Hg (ΔP_o ΔP_t) The increase which exists in these parameters (ΔV ΔP_o ΔP_t) at high intraocular pressure is therefore also highly significant as compared with the corresponding data in normotensive eyes As will be discussed later the indentation pulse is dependent on and caused by a pulsesynchronous change in ocular volume This volume

Table II

The normal corneal indentation pulse values obtained at various eye tension levels as measured with the 5.5 g plunger weight

Scale reading	Number of eyes N	Corneal indentation pulse recordings				
		μ	σ	ΔV	σ	t value †
10	3	38.7	14.43			
9.5	0					
9	1	25.0		3.30	1.18	0.221
8.5	1	30.0				
8	5	26.8	5.07	2.55	0.43	2.406 x
7.5	7	24.7	4.63	2.35	0.44	3.679 xxx
7	21	26.0	8.55	2.47	0.81	3.064 xx
6.5	22	28.0	10.46	2.69	1.00	1.873
6	37	30.1	7.31	2.92	0.71	
5.5	16	30.6	8.26	3.02	0.81	
5	45	31.8	10.12	3.18	1.01	
4.5	18	29.2	10.06	3.00	1.03	
4	22	33.2	13.31	3.49	1.40	
3.5	7	26.7	5.06	2.91	0.55	
3	11	39.2	16.55	4.43	1.87	2.141 x
2.5	9	47.9	16.37	5.06	1.93	2.848 xx
2	10	48.3	22.30	5.92	2.73	3.124 xx
1.5	3	39.3	16.04			
1	4	34.0	9.09	4.84	1.51	2.831 xx
0.5	3	42.0	20.30			
0	2	34.5	14.85	7.40	3.03	3.903 xxx
-1 ††	3	63.3	13.65			

† Student s t test employed by testing the various results against data obtained at R = 5

†† Converting values employed as for R = 0

Table I

Composition of material and results obtained in various groups of patients

Patient group	Number of eyes N	Mean intraocular pressure (mm Hg)		Amplitude (mean) μ	Standard deviation σ	Mean amplitude converted into		
		P_o	P_t			(mm³) ΔV	(mm Hg) ΔP_o	(mm Hg) ΔP_t
A	100	15 1	29 4	30 02	10 048			
B	27	18 4	32 1	29 85	9 746			
C	65	15 1	29 4	29 59	9 139			
D	13	19 5	33 1	29 69	9 223			
A+B+C+D	205	15 8	30 0	29 84	9 610	2 96	1 49	1 32
E	45	30 0	41 8	43 09	17 666	5 48	4 34	3 66

levels are listed with half a scale reading intervals in Table II and visualized in Fig 1 Fig 1 demonstrates that the increase in μ indentation pulse amplitu des at higher levels of intraocular pressure is comparatively smaller than the corresponding increase in mm³ (ΔV) and mm Hg (ΔP_o ΔP_t) The increase which exists in these parameters (ΔV ΔP_o ΔP_t) at high intraocular pressure is therefore also highly significant as compared with the corresponding data in normotensive eyes As will be discussed later the indentation pulse is dependent on and caused by a pulsesynchronous change in ocular volume This volume

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Scale reading	Number of eyes N	Corneal indentation pulse recordings				
		μ	σ	ΔV	σ	t value †
10	3	33 7	14 43			
9 5	0					
9	1	25 0		3 30	1 18	0 221
8 5	1	30 0				
8	5	26 8	5 07	2 55	0 48	2 406 x
7 5	7	24 7	4 68	2 35	0 44	3 679 xxx
7	21	26 0	8.55	2 47	0 81	3 064 xx
6 5	22	28 0	10 46	2 69	1 00	1 873
6	37	30 1	7 31	2 92	0 71	
5	16	30 6	8 26	3 02	0 81	
5	45	31 8	10 12	3 18	1 01	
4 5	18	29 2	10 06	3 00	1 03	
4	22	33 2	13.31	3 49	1 40	
3 5	7	26 7	5 06	2 91	0 55	
3	11	39 2	16 55	4 43	1 87	2 141 x
2 5	9	42 9	16 37	5 06	1 93	2 843 xx
	10	43 3	22 30	5 92	2 73	3 124 xx
1 5	3	39.3	16 04			
1	4	34 0	9 09	4 84	1 51	2 831 xx
0 5	3	42 0	20 30			
0	2	34.5	14 85	7 40	3 03	3 903 xxx
–1 ††	3	63 3	13 65			

† Student s t test employed by testing the various results against data obtained at R = 5

†† Converting values employed as for R = 0

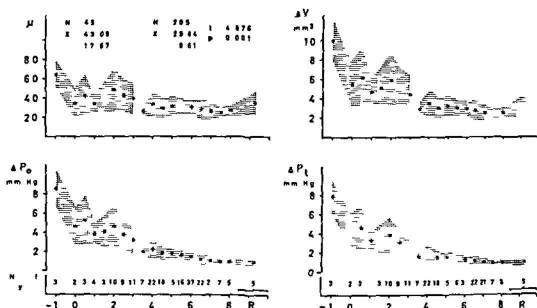


Fig 1

Corneal indentation pulse values obtained in μ ΔV ΔP_0 and ΔP_t at various eye tension levels as measured with the 5 5 g plunger weight in 250 human eyes
Shaded area = mean ± 1 σ

has been calculated at half a scale reading intervals and is listed in Table II The change in mm³ pulsatile volume (ΔV) obtained at various scale readings was compared with the value obtained at scale reading 5 ($\Delta V_{R=5}$) by use of the Students t test The various significance levels (x = 5 % xx = 1 % xxx = 0 1 %) is indicated in Table II by use of the symbol x adjacent to the listed t values As demonstrated a marked and significant increase of the pulsesynchronous change in ocular volume exists at an elevated intraocular pressure level of 37 57 mm Hg ($P_{tR=5} - P_{tR=-1}$) A less striking but still significant decrease in pulsatile volume exists at R = 7 – R = 8

The following conclusions may be drawn The corneal indentation pulse amplitude in microns of plunger movement is dependent on the eye tension level and will to some extent increase with decreasing values of R when the 5 5 g plunger weight is employed The corresponding pulsesynchronous variation in ocular volume will change in a fairly identical pattern The pulsesynchronous changes in intraocular pressure (ΔP_0 and ΔP_t) demonstrate a growing mm Hg increase with increasing levels of intraocular pressure (Fig 1) This increase is more pronounced than the increase in mm³ pulsatile volume a fact which is fully explained by the known pressure volume relationship of the eye as previously discussed

The present material offers possibilities of further information

Age distribution The corneal indentation pulse amplitudes in microns of plunger movement are plotted against the age of the 127 patients with normotensive eyes (A + B) and listed in Table III As demonstrated the indentation pulse amplitudes are of the same order of magnitude in subjects below 60 years of age At higher age a slight decrease in corneal indentation pulse amplitudes exists which probably reflects the more rigid arteries and arterioles in that age group compared with those of younger subjects The decrease is significant at the 1 % level as judged by the Students t test

Sex distribution The present material (A + B) consists of 78 females and 49 males A mean corneal indentation pulse amplitude of 31 4 μ (σ = 9 587) was obtained in the females compared with 27 7 μ (σ = 10 184) in the males This difference is significant at the 5 % level as judged by the Students t test No proper explanation of this fact is offered The difference in amplitudes between the two sexes is accepted with some reservations as the material was not primarily selected in order to study the sex relationship Thus the material contains 61 4 % females and 38 6 % males instead of the more preferrable 50 % of each group

The consistency of the recordings was studied in 33 patients (57 eyes) which were examined twice at various intervals from one day to several months The results are presented in Fig 2 which gives the amplitudes in microns of plunger movement of the first (x = abscissa) and the second (y = ordinate) examinations There is a definite correlation between the results of the two examinations fitting the equation y = 4 3894 + 0 8744 x A correlation coefficient of r = 0 8005 was obtained indicating a highly significant correlation between x and y (t = 6 635 P < 0 001) The various x values were also tested against the corresponding y values by use of the statistical method of paired comparison No significant difference between the x and y values of the same subject was demonstrated (t = 1 47) Accordingly the indentation pulse amplitude may be regarded as a rather constant and characteristic value in the one subject although large variations in amplitudes exist between the different subjects

Right eye – left eye comparison Fig 3 offers the corneal indentation pulse amplitude of the right eye (x = abscissa) plotted against the left eye value (y = ordinate) in 34 subjects which yielded identical and normal eye tension readings in their two eyes The data obtained fits the equation y = 0 1935 + 0 9913 x (r = 0 997) No significant difference between the two eyes of the same subject was demonstrated

Normotensive eyes with small differences in eye tension levels 31 subjects demonstrated a mean difference of R = 0 73 in eye tension between their two eyes i e a difference of 1 51 mm Hg intraocular pressure (P_t values $\bar{x}$ = 29 951 y = 28 438 mm Hg) Plotting the corneal indentation pulse amplitude from the eye with higher intraocular pressure (x = abscissa) against the eye

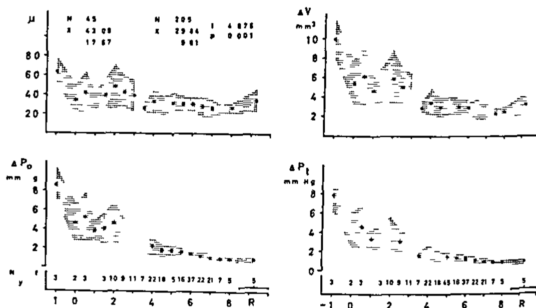


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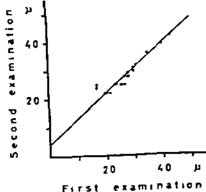


Fig 2

Consistency of corneal indentation pulse recordings obtained by examination of 57 eyes at intervals from 1 day to several months

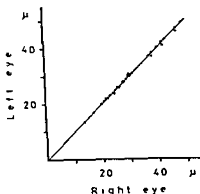


Fig 3

Corneal indentation pulse registration in right and left eye in 34 subjects

with lower intraocular pressure (y = ordinate) yields data fitting the equation y = 1 352 + 0 921 x (r = 0 984) The results are visualized in Fig 4 In the eyes with lower intraocular pressure the amplitudes were larger in 3 eyes of equal size in 13 and lower in 15 eyes which indicates that a slight reduction of the corneal indentation pulse amplitudes should be expected in the eye with lower intraocular pressure In the 31 subjects above yielding differences in eye tension between their two eyes of 2 scale readings or less this difference in

Table III

Corneal indentation pulse amplitudes in relation to age

Age	<10	10	20	30	40	50	60	70	80
N	2	7	12	10	21	33	22	16	4
$\bar{x}$	20 50	32 14	31 33	29 70	31 05	32 98	27 86	26 50	24 00
σ	0 71	10 57	10 29	10 11	10 20	12 03	7 61	7 07	3 27
N		21			64			42	
x		30 57			31 78			26 98	
σ		10 16	t = 0 463		11 07	t = 2 726 xx		7 08	

N = number of patients $\bar{x}$ = mean corneal indentation pulse amplitude in μ σ = standard deviation

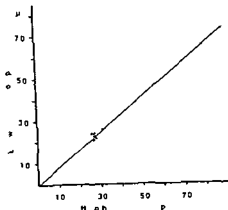


Fig 5
Corneal indentation pulse recordings in 27 glaucoma patients with a pronounced difference in eye tension between their two eyes

pressure (x = abscissa) was plotted against the amplitude of the eye with lower intraocular pressure (y = ordinate) and the results are presented in Fig 5 The data obtained fitted the equation $y = -0.487 + 0.835\ x$ $(r = 0.94)$ which indicates that an average reduction in amplitude of about 17 % exists in the eyes with lower intraocular pressure of these 27 glaucoma patients This difference in corneal indentation pulse amplitude between the two eyes in the same subject is highly significant ($P < 0.001$) as judged by the Wilcoxon Signed ranks test and confirms the results presented in Table II and discussed above

Comparison of amplitudes recorded in the same eye at various eye tension levels In order to study the possible difference in corneal indentation pulse amplitudes in normotensive eyes with differences in eye tension exceeding 2 scale readings Schiøtz tonography was performed in 15 normal eyes (14 subjects) By use of the calibrated zero suppression equipment of our Mark 280 recorder the tracings may be kept on the running paper even when the sensitivity is increased as demonstrated in Fig 6 Accordingly the corneal indentation pulse amplitudes may be measured with sufficient degree of accuracy at the start and end point of the tonography procedure The results obtained are presented in Table IV The average intraocular pressure in the 15 eyes was 30 14 mm Hg (P_t) at start and 25 08 mm Hg (P_t) at the end of tonography A highly significant decrease was demonstrated in corneal indentation pulse amplitudes and in pulsesynchronous change in ocular volume (ΔV) as judged by the statistical method of paired comparison Accordingly during tonography not only will the corneal indentation pulse demonstrate a significant reduction in ampli

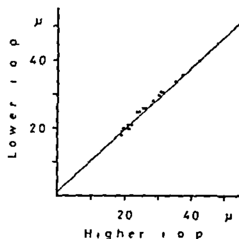


Fig 4
Corneal indentation pulse recordings in 31 subjects with different eye tension levels in their normotensive eyes

amplitude was significant at the 1 % level as judged by the Wilcoxon Signed ranks test

Normally therefore a certain difference in corneal indentation pulse amplitude between the two eyes of the same subject may be expected because a difference in eye tension of up to 2 scale readings Schiotz may exist In order to evaluate the magnitude of this difference in amplitudes between the two eyes in the same subject the 65 subjects mentioned above (C) which had both of their eyes examined were studied in detail The difference in amplitude between the two eyes was recorded in per cent positive valuest indicate larger amplitude of right eye negative values indicate larger amplitude of left eye The differences yielded a normal frequency distribution and varied between −8 51 and +16 67 % with an arithmetical mean of $\bar{x}$ = +1 20 % (σ (of population) = 4 61) This indicates that only 0 27 % of the population will yield differences beyond $\bar{x} \pm 3$ σ i e beyond −12 63 and +15 03 % Accordingly the corneal indentation pulse amplitudes are of a similar order of magnitude in the two eyes of the same subject a repeated difference of ± 15 % or more is considered as a definite pathological finding

Glaucomatous eyes with larger differences in eye tension levels Most probably a significant difference in amplitudes may be demonstrated between the two eyes also when a more pronounced and pathological difference exists between their intraocular pressures 27 glaucoma patients demonstrated a mean difference in intraocular pressure of 6 74 mm Hg (P_t values $\bar{x}$ = 41 088 $\bar{y}$ = 34 345) i e a mean difference in eye tension of R = 1 91 between their two eyes The corneal indentation pulse amplitude of the eye with larger intraocular

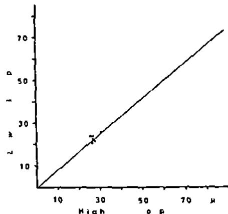


Fig 5
Corneal indentation pulse recordings in 27 glaucoma patients with a pronounced difference in eye tension between their two eyes

pressure (x = abscissa) was plotted against the amplitude of the eye with lower intraocular pressure (y = ordinate) and the results are presented in Fig 5 The data obtained fitted the equation $y = -0.487 + 0.835 \; x$ ($r = 0.94$) which indicates that an average reduction in amplitude of about 17 % exists in the eyes with lower intraocular pressure of these 27 glaucoma patients This difference in corneal indentation pulse amplitude between the two eyes in the same subject is highly significant ($P < 0.001$) as judged by the Wilcoxon Signed ranks test and confirms the results presented in Table II and discussed above

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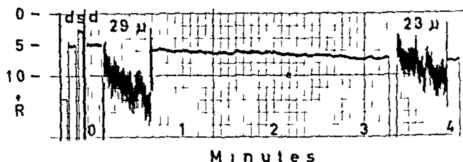


Fig 6

Corneal indentation pulse recordings during tonography

tude the pulsesynchronous change in ocular volume will also decrease along with decreasing intraocular pressure

Indentation pulse amplitudes at higher levels of intraocular pressure This problem was studied in some patients not listed above The corneal indentation pulse was studied at various eye tension levels by use of the 5 5 and 10 g plunger weights during the period of treatment of 3 patients suffering from acute glaucoma Although the results were not identical in all cases a definite tendency was recognized At high intraocular pressures (P_t = 70 90 mm Hg) rather small indentation pulse amplitudes were recorded The amplitudes increased however with decreasing intraocular presure until a maximum value was obtained at 40 50 mm Hg (P_t) At lower intraocular pressures a marked decrease was found

The corneal indentation pulse was also examined in a female patient suffering from secondary glaucoma in her left eye caused by lens luxation into the anterior chamber The corneal indentation pulse amplitude was zero at an intraocular pressure of 93 4 mm Hg (P_t) Following lens extraction with subsequent decrease in intraocular pressure the amplitudes recovered to subnormal values although the eye was amaurotic

The indentation pulse amplitude pattern evaluated in these patients may not however reflect the pattern in normal eyes as the disease itself may have influenced the blood supply to the eye The indentation pulse should therefore be recorded at short intervals at different intraocular pressure levels in the same patient This was obtained in two ways

First the indentation pulse amplitudes were recorded with the 5 5 and 10 g plunger weight in the same eye This was done in 90 eyes and the results are presented in Table V At lower intraocular pressure levels the amplitudes are slightly larger when recorded with the 10 g plunger weight the difference is not however statistically significant At higher intraocular pressure levels the amplitudes obtained with the 10 g plunger weight are considerably decreased

Table IV

Average values obtained by tonography in 15 eyes A highly significant decrease in corneal indentation pulse amplitudes intraocular pressure and pulse synchronous change in ocular volume (ΔV) is observed

Scale reading (R)		Amplitude (a)		Intraocular pressure (P_t) (mm Hg)			(ΔV) (mm³)		
Start	End	Start	End	Start	End	Difference	Start	End	Difference
5 67	8 90	26 13	22 13	30 14	25 08	5 06	2 615	2 131	0 484
		P < 0 001				P < 0 001			P < 0 001

Table 1

Corneal indentation pulse recorded with 5.5 g and 10 g plunger weights at various eye tension levels (N = number of eyes R = scale reading Schiøtz (mean) $\bar{x}$ = indentation pulse amplitude in μ (mean))

N	2	4	5	10	8	19	13	16	10	2	1
$R_{5.5}$	−1	0	1	2	3	4	5	6	7	8	9
R_{10}	3.8	4.9	6	6.8	7.9	8.8	9.6	10.9	11.6	12.8	13.5
$\bar{x}_{5.5}$	45.5	37.5	42.8	40.7	32.9	29.9	31.2	34.8	27.0	32.5	24.0
$\bar{x}_{10}$	27.0	26.8	34.4	40.6	32.0	29.8	33.0	35.9	26.9	33.5	25.0
$\bar{x}_{5.5}-\bar{x}_{10}$	18.5	10.7	8.4	0.1	0.9	0.1	−1.8	−1.1	0.1	−1.0	−1.0

N	11
$\bar{x}_{5.5}$	41.363
$\bar{x}_{10}$	30.272
$\bar{x}_{5.5}-\bar{x}_{10}$	11.091
t value	2.301 xx

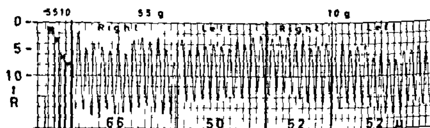


Fig 7

Corneal indentation pulse amplitudes recorded with 5.5 g and 10 g plunger weights A decrease in amplitude is demonstrated in right eye when the 10 g plunger weight is employed

as shown in Fig 7 This difference between the 5.5 g and 10 g recordings is significant at the 1 % level as judged by the Students t test

Second the indentation pulse was recorded in a choroidal melanoma eye at various levels of intraocular pressure obtained by injection of 0.9 % saline into the anterior chamber followed by subsequent aspiration of fluid The experiment was performed under topical anesthesia (oxibuprocain) The indentation pulse amplitudes obtained at various levels of intraocular pressure (P_i) are visualized in Fig 8 and Fig 9 In the latter the corresponding pulsesynchronous

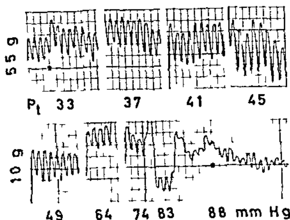


Fig 8
Corneal indentation pulse recorded at various levels of intraocular pressure (P_t) in a canulated melanoma eye Sensitivity 2 mV = 2 μ per paper division

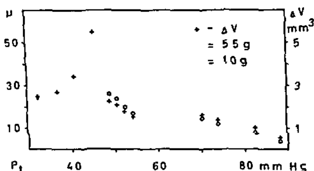


Fig 9
Corneal indentation pulse values in μ plunger movements and mm³ change in intra ocular volume demonstrated at various levels of intraocular pressure in a canulated melanoma eye

change in ocular volume is also given The results of this experiment confirm in every way what has been found by dynamic tonometry in the *clinical* material presented above

Table V

Corneal indentation pulse recorded with 5.5 g and 10 g plunger weights at various eye tension levels (N = number of eyes R = scale reading Schiotz (mean) x = indentation pulse amplitude in μ (mean))

N	2	4	5	10	8	19	13	16	10	2	1
$R_{5.5}$	– 1	0	1	2	3	4	5	6	7	8	9
R_{10}	3.8	4.9	6	6.8	7.9	8.8	9.6	10.9	11.6	12.8	13.5
$\bar{x}_{5.5}$	45.5	37.5	42.8	40.7	32.9	29.9	31.2	34.8	27.0	32.5	24.0
$\bar{x}_{10}$	27.0	26.8	34.4	40.6	32.0	29.8	33.0	35.9	26.9	33.5	25.0
$\bar{x}_{5.5}-\bar{x}_{10}$	18.5	10.7	8.4	0.1	0.9	0.1	– 1.8	– 1.1	0.1	– 1.0	– 1.0

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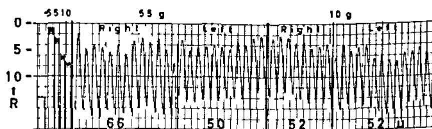


Fig 7

Corneal indentation pulse amplitudes recorded with 5.5 g and 10 g plunger weights A decrease in amplitude is demonstrated in right eye when the 10 g plunger weight is employed

as shown in Fig 7 This difference between the 5.5 g and 10 g recordings is *significant at the 1 % level as judged by the Students t test*

Second the indentation pulse was recorded in a choroidal melanoma eye at various levels of intraocular pressure obtained by injection of 0.9 % saline into the anterior chamber followed by subsequent aspiration of fluid The experiment was performed under topical anesthesia (oxibuprocain) The indentation pulse amplitudes obtained at various levels of intraocular pressure (P_t) are visualized in Fig 8 and Fig 9 In the latter the corresponding pulsesynchronous

pulse amplitude The amplitudes will change corresponding to the various levels of intraocular pressure whether the eye is glaucomatous or not Accordingly adequately treated glaucomatous eyes with intraocular pressure within normal range will yield normal sized corneal indentation pulse amplitudes And normal eyes examined during artificial elevation of intraocular pressure will yield an increase in corneal pulse amplitude which may be compared with the increase observed in hypertensive glaucomatous eyes

As known a certain pulsation in venous pressure exists in the jugular vein being initiated from the right auricle Compared with the pulsesynchronous change in mm Hg intraarterial pressure this venous pulsation is negligible Accordingly the bulk of fluid (blood aqueous humor) which leaves the eye during the systole and diastole will do so at a rather constant speed The blood will however enter the eye mainly during the systole and only to a much lesser extent during the diastole When the bulk of blood which enters the eye during diastole (D) is subtracted from the bulk of blood entering the eye in systole (S) the difference (S – D) may be called the excess of blood which enters the eye during systole This volume ($\Delta V = S - D$) will initiate the pulsation in intraocular pressure and may be calculated from the recorded corneal indentation pulse amplitude in microns of plunger movement by use of the convertion table previously presented (*Horven* 1960) It is stressed that the corneal indentation pulse will reflect the excess of blood entering the eye in systole (S – D) and not the bulk of blood which flows through the eye during one heart cycle (S + D) Accordingly true values of the bulk of blood which flows through the eye during one heart cycle may be obtained only under the prerequisite that D is zero a situation which possibly exists when the intraocular pressure equals the diastolic blood pressure of the ophthalmic artery If the intraocular pressure exceeds the diastolic blood pressure blood may enter the eye in systole and to some extent return to the ophthalmic artery in diastole in which case D *will* be negative Under these circumstances the bulk of blood which flows through the eye will be less than expected from the indentation pulse recordings as the negative D will participate with S in initiating the pulsations in intraocular pressure Theoretically therefore if the intraocular pressure and the peripheral vascular resistance were very high most of the blood entering the eye in systole would not be able to pass into the capillaries and veins On the contrary a backflow of blood would exist forcing the blood into the ophthalmic artery again Thus at high levels of intraocular pressure a fair corneal indentation pulse amplitude *may* be recorded as a consequence of this forward backwards movement of blood in the arterioles while the bulk of blood flowing through the capillaries and veins and supporting the nourishment of the eye may be rather negligible and insufficient *This view was recently supported by* experimental studies in farm pigs (*Dollery et al* 1968) By use of cine fluorescence angiograms a substantial backflow of blood in the retinal arterioles in

Discussion

The results obtained demonstrate that the corneal indentation pulse amplitudes in microns of plunger movement are related to the intraocular pressure level In normotensive eyes (P_t average 30 07 mm Hg) the mean pulsesynchronous change in indentation pulse amplitude was 29 84 μ which corresponds to a change in ΔV of 2 96 mm^3 in ΔP_t of 1 32 mm Hg and in ΔP_0 of 1 49 mm Hg In hypertensive eyes these values were significantly increased In one of their normal cases *Bron et al* (1967) offer a ΔV value of 2 1 mm^3 This value was calculated by use of Friedenwald s data which yields results of about 70 % of the Langham – Hetland Eriksen convertion table used in the present study If *Bron et al* (1967) had employed the convertion table used in this study a ΔV value of 3 0 mm^3 would have been demonstrated which actually is identical with the mean value of 2 96 mm^3 obtained in the present study The reason why Langham – Hetland Eriksen s data are preferred for convertion of corneal indentation pulse amplitudes in microns into corresponding mm^3 change in ocular volume is discussed in detail elsewhere (*Hørven* 1970)

Lawrence & Schlegel (1966) demonstrated in rabbits a ΔV value of 0 4 0 7 mm^3 which did not change with the intraocular pressure level The corresponding pulsesynchronous change in intraocular pressure varied between 0 2 mm Hg (normotensive eyes) and 2 0 mm Hg (hypertensive eyes) Identical results were presented by *Bynke* (1968) Thus the values reported from rabbits are only 20 30 % of those obtained in man This discrepancy is probably not caused by the difference in species but by the fact that these animals were examined under general anesthesia In man the indentation pulse amplitudes and the corresponding changes in ocular volume are reduced to about 30 % of their normal values during general anesthesia (*Hørven & Syrdalen* 1970) and preliminary experiments on rabbits are confirmative with this observation (*Hørven* 1968 b) Results concerning the pulsesynchronous change in intraocular pressure and volume obtained in animals (and man) during general anesthesia should therefore be accepted with a large part of skepticism Such results will not reflect the normal state of non anesthetised animals As mentioned above the indentation pulse amplitude reaches its maximum at an elevated intraocular pressure of 37 57 mm Hg At higher intraocular pressures the amplitudes decrease until zero values when the intraocular pressure exceeds the systolic pressure of the ophthalmic artery This pattern of indentation pulse amplitude behavior was demonstrated in acute glaucoma chronic simple glaucoma and capsular glaucoma eyes as well as in eyes with normal outlet channels for the aqueous humor In these latter eyes the elevated intraocular pressure was obtained either experimentally by injection of fluid into the eye or by a luxated lens which temporarely blocked the chamber fluid drainage The following conclusions may be drawn the glaucomatous disease per se does not alter the corneal indentation

pulse amplitude The amplitudes will change corresponding to the various levels of intraocular pressure whether the eye is glaucomatous or not Accordingly adequately treated glaucomatous eyes with intraocular pressure within normal range will yield normal sized corneal indentation pulse amplitudes And normal eyes examined during artificial elevation of intraocular pressure will yield an increase in corneal pulse amplitude which may be compared with the increase observed in hypertensive glaucomatous eyes

As known a certain pulsation in venous pressure exists in the jugular vein being initiated from the right auricle Compared with the pulsesynchronous change in mm Hg intraarterial pressure this venous pulsation is negligible Accordingly the bulk of fluid (blood aqueous humor) which leaves the eye during the systole and diastole will do so at a rather constant speed The blood will however enter the eye mainly during the systole and only to a much lesser extent during the diastole When the bulk of blood which enters the eye during diastole (D) is subtracted from the bulk of blood entering the eye in systole (S) the difference (S – D) may be called the excess of blood which enters the eye during systole This volume ($\Delta V \approx S - D$) will initiate the pulsation in intraocular pressure and may be calculated from the recorded corneal indentation pulse amplitude in microns of plunger movement by use of the convertion table previously presented (*Horven* 19,0) It is stressed that the corneal indentation pulse will reflect the excess of blood entering the eye in systole (S – D) and not the bulk of blood which flows through the eye during one heart cycle (S + D) Accordingly true values of the bulk of blood which flows through the eye during one heart cycle may be obtained only under the prerequisite that D is zero a situation which possibly exists when the intraocular pressure equals the diastolic blood pressure of the ophthalmic artery If the intraocular pressure exceeds the diastolic blood pressure blood may enter the eye in systole and to some extent return to the ophthalmic artery in diastole in which case D will be negative Under these circumstances the bulk of blood which flows through the eye will be less than expected from the indentation pulse recordings as the negative D will participate with S in initiating the pulsations in intraocular pressure Theoretically therefore if the intraocular pressure and the peripheral vascular resistance were very high most of the blood entering the eye in systole would not be able to pass into the capillaries and veins On the contrary a backflow of blood would exist forcing the blood into the ophthalmic artery again Thus at high levels of intraocular pressure a fair corneal indentation pulse amplitude may be recorded as a consequence of this forward backwards movement of blood in the arterioles while the bulk of blood flowing through the capillaries and veins and supporting the nourishment of the eye may be rather negligible and insufficient This view was recently supported by experimental studies in farm pigs (*Dollery et al* 1968) By use of cine fluorescence angiograms a substantial backflow of blood in the retinal arterioles in

The results obtained demonstrate that the corneal indentation pulse amplitudes in microns of plunger movement are related to the intraocular pressure level In normotensive eyes (P_t average 30 07 mm Hg) the mean pulsesynchronous change in indentation pulse amplitude was 29 84 μ which corresponds to a change in ΔV of 2 96 mm³ in ΔP_t of 1 32 mm Hg and in ΔP_o of 1 49 mm Hg In hypertensive eyes these values were significantly increased In one of their normal cases *Bron et al* (1967) offer a ΔV value of 2 1 mm³ This value was calculated by use of Friedenwald s data which yields results of about 70 % of the Langham – Hetland Eriksen convertion table used in the present study If *Bron et al* (1967) had employed the convertion table used in this study a ΔV value of 3 0 mm³ would have been demonstrated which actually is identical with the mean value of 2 96 mm³ obtained in the present study The reason why Langham – Hetland Eriksen s data are preferred for convertion of corneal indentation pulse amplitudes in microns into corresponding mm³ change in ocular volume is discussed in detail elsewhere (*Horven* 1970)

Lawrence & Schlegel (1966) demonstrated in rabbits a ΔV value of 0 4 0 7 mm³ which did not change with the intraocular pressure level The corresponding pulsesynchronous change in intraocular pressure varied between 0 2 mm Hg (normotensive eyes) and 2 0 mm Hg (hypertensive eyes) Identical results were presented by *Bynke* (1968) Thus the values reported from rabbits are only 20 30 % of those obtained in man This discrepancy is probably not caused by the difference in species but by the fact that these animals were examined under general anesthesia In man the indentation pulse amplitudes and the corresponding changes in ocular volume are reduced to about 30 % of their normal values during general anesthesia (*Horven & Syrdalen* 1970) and preliminary experiments on rabbits are confirmative with this observation (*Horven* 1968 b) Results concerning the pulsesynchronous change in intraocular pressure and volume obtained in animals (and man) during general anesthesia should therefore be accepted with a large part of skepticism Such results will not reflect the normal state of non anesthetised animals As mentioned above the indentation pulse amplitude reaches its maximum at an elevated intraocular pressure of 37 57 mm Hg At higher intraocular pressures the amplitudes decrease until zero values when the intraocular pressure exceeds the systolic pressure of the ophthalmic artery This pattern of indentation pulse amplitude behavior was demonstrated in acute glaucoma chronic simple glaucoma and capsular glaucoma eyes as well as in eyes with normal outlet channels for the aqueous humor In these latter eyes the elevated intraocular pressure was obtained either experimentally by injection of fluid into the eye or by a luxated lens which temporarely blocked the chamber fluid drainage The following conclusions may be drawn the glaucomatous disease per se does not alter the corneal indentation

Summary

Corneal indentation pulse registrations have been performed by use of dynamic tonometry in 205 normotensive and 45 hypertensive human eyes In addition to evaluate the age and sex distribution the normal values of indentation pulse amplitudes are given at various eye tension levels Normally the indentation pulse amplitudes are of the same order of magnitude in the two eyes of the same subject a difference of ± 15 % or more between the two eyes is considered as a definite pathological finding

Acknowledgment

The skilful technical assistance of Mrs Gull Britt Huseby is gratefully acknowledged

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diastole was demonstrated Experimental studies demonstrate also that an artificial elevation of intraocular pressure will cause a reduction in the amount of blood in the choroid (*Broadfoot et al* 1961) and a reduced rate of blood flow through the uvea (*Bill* 1962)

Of course if the intraocular pressure exceeds the systolic pressure in the ophthalmic artery no blood will enter the eye the indentation pulse amplitude will be zero and the eye will turn amaurotic as demonstrated above in the case with luxated lens A zero indentation pulse amplitude may however also be recorded when a certain and presumably sufficient bulk of blood flows through the vascular bed of the eye if this blood flow is non pulsatile, i e if S = D Clinically this has been observed in two conditions During general anesthesia a zero indentation pulse amplitude has been recorded in both eyes of one patient (*Horven & Syrdalen* 1970) In giant cell arteritis a zero or close to zero indentation pulse amplitude has been recorded by several occations in eyes with normal or only slightly reduced vision (*Horven* 1969 b) This latter observation is in complete agreement with the findings of *Conrad & Green* (1964) They demonstrated that the ratio of flow to pulse was markedly elevated in patients with peripheral arterial occlusive disease In normotensive eyes the blood most probably flows continuously into the eye in diastole yielding a positive D If so the bulk of blood which flows through the vascular bed of the eye will exceed the mm^3 change in ocular volume calculated from the recorded indentation pulse amplitude Thus counting 72 heart beats in a minute the blood flow through the average normal human eye should exceed 0 213 ml per minute (i e 72 2 96 mm^3)

In order to explain the change in magnitude of the indentation pulse amplitude and ΔV which exists at various levels of intraocular pressure it is easily understood that a decrease should occur with increasing intraocular pressure at high levels of intraocular presure because less blood will enter the eye during these circumstances More difficult to explain is the fact that a maximum value exists at 37 57 mm Hg intraocular pressure below this level a decrease in amplitude and ΔV occurs with decreasing intraocular pressure as demonstrated above One possible explanation may be that the pulsatile vascular bed increases with increasing intraocular pressures up to a level of 37 57 mm Hg Whether the increase in pulsatile vascular bed is initiated by opening of shunts or by stretching of the eye wall and longitudinal extension of the arterioles is unknown It is known however that in pathological conditions as choroidal melanomas (*Horven* 1969 a) and Sturge Webers disease (*Flage & Horven* 1970) where the pulsatile uveal vascular bed is increased a corresponding increase is obtained also in the corneal indentation pulse amplitude

Summary

Corneal indentation pulse registrations have been performed by use of dynamic tonometry in 205 normotensive and 45 hypertensive human eyes In addition to evaluate the age and sex distribution the normal values of indentation pulse amplitudes are given at various eye tension levels Normally the indentation pulse amplitudes are of the same order of magnitude in the two eyes of the same subject a difference of ± 15% or more between the two eyes is considered as a definite pathological finding

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CORNEAL INDENTATION PULSE AND GENERAL ANESTHESIA

BY

IVAR HØRVEN and PER SYRDALEN

Most of the experimental work previously done in animals in order to study the ocular blood supply and hydrodynamics has been performed during general anesthesia It is quite possible however that the general anesthesia itself to some extent may influence the various factors responsible for the ocular blood supply such as blood pressure intraocular pressure and the peripheral vascular resistence In order to investigate this possibility dynamic tonometry (*Hørven* 1968) was performed during Nembutal (pentobarbital sodium) anesthesia on two rabbits by one of us (I H) with a corneal pulse amplitude recorded close to zero as a result

This preliminary finding initiated the present study which offers the results obtained by dynamic tonometry performed before following premedication and during general anesthesia in human beings

Material

The material consists of 24 patients suffering from various eye diseases as strabism (11) retinal detachment (6) glaucoma (7) choroidal melanoma (2) extra

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ocular tumors (2) and ptosis (1) The normal mate eye was studied and when possible the affected eye was also included yielding a total of 39 eyes The age of the patients averaged 27 years (5 67) there were 11 males and 13 females

Methods

On the day of surgery dynamic tonometry was performed before following premedication and during general anesthesia Some of the patients got their premedication early in the morning before examination could be performed The group of patients examined before premedication counts therefore only 11 subjects (18 eyes) In the first two cases (4 eyes) dynamic tonometry was per formed before premedication and during general anesthesia Later on it was found preferable also to include an examination following premedication which was done in the remaining 22 patients (35 eyes)

Dynamic tonometry is performed during topical anesthesia (oxibuprocain) just like an ordinary Schiotz tonometry The dynamic tonometer is made ac cording to the known principles of electronic tonometers with certain important modifications (*Horven* 1968) In its present state the tonometer yields an output of 1 mV per 1 μ plunger deflection An output of 50 mV therefore corresponds to a plunger movement of 50 μ which equals one scale reading Schiotz When high sensitivity is employed the tracings may be kept on the running paper by use of a zero suppression unit thus offering the possibility to study the corneal indentation pulse amplitudes with a sufficient degree of accuracy Normally the amplitudes are of the same order of magnitude in the two eyes and average about 30 μ of plunger movement i e about 0 6 scale reading Schiotz (*Horven* 1970 b)

Premedication In adults a slight sedative effect was obtained by use of the phenothiazine derivatives Phenergan (promethazine) 25 mg or Pacatal (mepa zine) 100 mg given orally one hour prior to general anesthesia In children a more pronounced sedation was obtained by use of Seconal (meballymal) 100 150 mg given orally one hour prior to general anesthesia Intramuscular admi nistration of atropine was employed in all cases

General anesthesia In most of the cases general anesthesia was initiated by intravenous injection of Thiopentone (thiomebumal) 150 400 mg followed by Curacit (succinyl choline) 40 80 mg and in *all* cases endotracheal tubing The general anesthesia was maintained by Halothane (fluothane) N O O or in some cases by ether In a few cases barbiturates and succinyl choline were not employed the general anesthesia being initiated and continued by ether and later on switched over to Halothane N O O

Results

he results obtained are summarized in Table I The eye tension was converted nto mm Hg intraocular pressure by use of Friedenwald s 1955 P_0 converting able and the pulsesynchronous change in mm³ ocular volume (ΔV) was calcu ated from the corneal indentation pulse amplitudes by use of Langham Het and Eriksen s data as previously described (*Horven* 1970 a)

A marked and striking decrease in corneal pulse amplitudes and correspond ng changes in ocular volume was demonstrated during general anesthesia No difference existed between ether and Halothane in this respect The decrease in corneal indentation pulse amplitudes was present in all but one of the cases studied In this one case no change in amplitudes was noted wheras in another case the amplitudes were actually recorded to be zero in both eyes Most of the cases demonstrated a marked decrease in both eyes to an average of about 33 %

Table I

Corneal indentation pulse amplitude (μ) pulsesynchronous change in ocular volume (ΔV) and intraocular pressure in mm Hg (P) recorded before premedication following premedication and during general anesthesia

		Mean	σ	%	t value
Before	μ	31 44	1? ?92	100	
premed cation	ΔV	3 30	1 63	100	
(N = 18)	P	17 9	6 6?3	100	
Phenergan	μ	33 00	18 5 6	105	0 247
Atropine	ΔV	3 9	3 015	1?0	0 654
(N = 11)	P	18 66	11 794	108	0 3[illegible]
Pacatal	μ	6 38	[illegible] 170	84	1 31[illegible]
Atr pine	ΔV	? 50	0 53	[illegible]	1 613
(N 8)	P	15 63	1 887	90	0 978
Seconal	μ	18 13	3 04[illegible]	58	3 776 xxx
Atropine	ΔV	1 9	0 7 9	54	3 ?93 xx
(N 16)	P_0	1[illegible] 06	?.564	93	0 [illegible]9
General	μ	10 43	7.383	33	6 [illegible]18 xxx
anesthesia	ΔV	1 08	0 91	33	5 100 xxx
(N 31)	P	13 38	6 375	77	? 098 x

S gn f ance levels x – xx = 1 % xxx = 0 1 %

of the normal preanesthetic value As judged by the Student s t test this decrease was significant at the 0 1 % level

A significant decrease in corneal indentation pulse amplitudes was also initiated by premedication with Seconal while Phenergan and Pacatal yielded smaller and non significant changes in the corneal pulse amplitudes

During general anesthesia a small decrease was also noted in the intraocular pressure with a mean P_0 value of 17 29 mm Hg before premedication compared with 13 38 mm Hg during general anesthesia This will roughly correspond to eye tension levels of scale reading 5 0 before premedication and 6 5 during general anesthesia as measured by the 5 5 g plunger weight

A typical recording is demonstrated in Fig 1 which shows the change in corneal pulse amplitudes caused by Seconal This patient was almost asleep when the recording was performed In patients with only a slight effect following Seconal administration the corresponding decrease in corneal pulse amplitudes was less pronounced

Fig 2 shows the tachycardia induced by preoperative atropine and the decrease in corneal pulse amplitudes caused by ether and later on by Halothane general anesthesia Barbiturates were not given in this case

Fig 3 demonstrates the effect of intravenous injection of Thiopentone on the corneal pulse amplitudes As the patient falls asleep the amplitudes yield a corresponding significant decrease Change in blood pressure or intraocular pressure levels may not be responsible for the decrease in corneal indentation pulse amplitudes which exists during general anesthesia as these parameters were unchanged in this case and other cases When a very deep anesthesia level

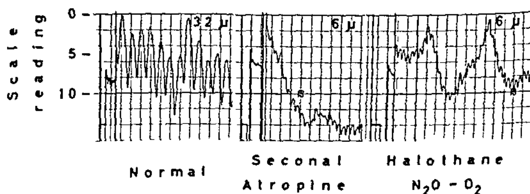


Fig 1

Decrease in corneal indentation pulse amplitudes induced by Seconal and maintained by Halothane N O O Sensitivity settings 20 and 2 mV per paper division

A

B



Fig 3

Case 1 14 vision 0 5 *A* A slight indication of a wheel like formation in the macula
B Angiogram showing intact pigment epithelium in the macula



C



B



A

Fig 10

Case 8 34, vision 0 1 *A* Retinal vascula veil, patches of atrophic pigment epi thelium *B* *Peripherally of the veil* a fluorescent vein is seen (arrow) the blood in the main trunk is in part non fluor escent The blood coming from the veil is poor in fluorescein The large vessels of the choroid are clearly visible



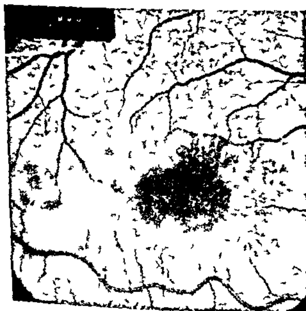


Fig 4

Case 9 29 vision 1 0 *A* A definite wheel like formation and perimacular radiate streaks *B* Angiogram showing normal pigment epithelium

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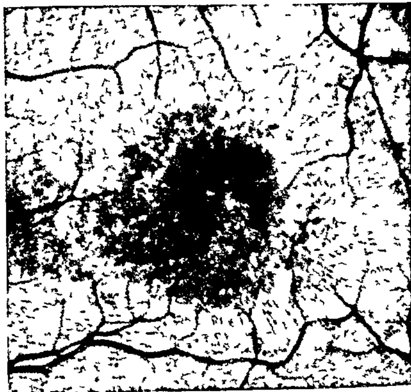
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A



B

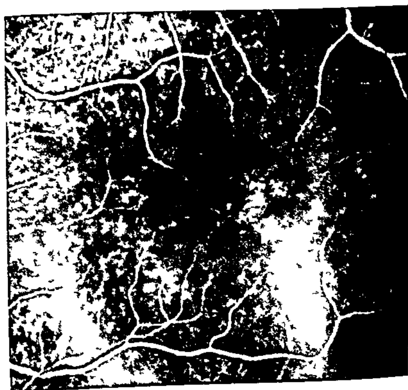


Fig 5

Case 3, 19, vision 0 7 *A* Moderately severe macular changes *B* Angiogram showing defects in the pigment epithelium

IMMUNHISTOLOGICAL STUDIES ON HUMAN DIABETIC AND NON DIABETIC EYES

I Fluorescent labelling of insulin and insulin antibodies

By

A U Werner and H -W Larsen

Published in *Acta Ophthalmologica*, 47 (1969) 937–955

IMMUNHISTOLOGICAL STUDIES ON HUMAN DIABETIC AND NON-DIABETIC EYES

II Autoradiography using I^{125} labelled insulin, and application of histochemical procedures

By

H -W Larsen and A U Werner

Published in *Acta Ophthalmologica*, 47 (1969) 956–971

Discussion

B Rosengren (Gothenburg)

Some years ago an elderly sanatorium physician mentioned that he had never seen retinopathia diabetica in a patient with pulmonary t b In my private practice I have endeavoured to ascertain whether there is evidence for a negative correlation between the diseases mentioned What I have found is two patients with t b of long standing who have had diabetes for about 35 years In neither case could any modification of the eye ground be detected by ordinary ophthalmoscopy Possibly the method mentioned would be capable of casting light on the question of a possible relationship





Fig 6

Case 4 44 vision finger counting 4 5m *A* Atypical coarsely granular destruction of the macula *B* Angiogram in which the choroid shows through

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INTRAOCULAR FEEDBACK MECHANISMS OF THE INTRAOCULAR PRESSURE IN RABBITS

By

Hallvard Valebjørg

Introduction

Pseudofacility' was defined by Bárány (1963 1967) as the number of μl/min by which the aqueous humor formation in the eye is reduced for every mm Hg pressure rise This is a facility which does not help outflow One factor in the pseudofacility is the decreased ultrafiltration rate as a consequence of the increased intraocular pressure Bárany suggested that there may perhaps be more mechanisms by which fluid production could become pressure sensitive If they exist, they contribute to pseudofacility'

The pseudofacility may be considered a negative feedback mechanism By use of a new method posterior bulbus fenestration which allows a direct inspection in vivo of the vessels of the ciliary body and the choroid in the rabbit (Valebjørg 1963, 1970a), various vascular changes have been observed during artificially raised intraocular pressure Based on these vascular responses three different feedback mechanisms have been postulated one of which results in a reduced aqueous formation and is thus included in the pseudofacility

A feedback mechanism may be defined as a process in which a fraction of the output is returned to the input stage (Fig 1)

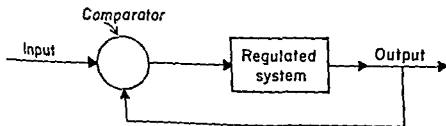


Fig 1
The principle of feedback systems.

A simple example is provided by the servo-assisted motor If the decrease or increase in speed of rotation is regulated in such a way that the system is brought nearer to a given speed (Sollwert) the process is called



A



B



C

Fig 7

Case 5 68, vision finger counting 3 5m *A* Localized macular process *B* Stronger fluorescence temporally *C* Large choroidal (?) blood vessel the strongest fluorescence is seen nasally

negative feedback. Positive feedback, on the other hand, would respond to an increase in speed of rotation by a further increase, and so on, yielding an unstable system.

Two important factors influence the intraocular volume and therefore the intraocular pressure:

(1) The volume of the intraocular blood vessels.

(2) The volume of the aqueous humor produced across the blood aqueous barrier per unit time. This production is achieved by processes of ultrafiltration, secretion and diffusion (Kinsey and Reddy 1964).

Material and methods

The results presented are based on observations in 7 eyes of adult albino rabbits in which the ciliary epithelium is almost devoid of pigment, and the underlying blood vessels therefore can easily be studied by the method of posterior bulbus fenestration. The animals were anesthetized with a mixture of chloralose and urethane. The intraocular pressure, recorded via a cannula inserted through the cornea, and the systemic blood pressure were measured continuously throughout the experiments. Variation in intraocular pressure was effected by alteration of the height of a saline reservoir connected to a second cannula inserted into the anterior chamber through the cornea.

Results

(1) Vascular negative feedback mechanism. — After completion of surgery the resting level of the intraocular pressure was about 15 mm Hg. Elevation of the intraocular pressure from 15 to 19–20 mm Hg caused a narrowing of the capillaries, the venules and the marginal veins of the ciliary processes (translental inspection) as well as of the choroidal veins (retrolental inspection). At higher pressure there was also a narrowing of the arterioles of the ciliary processes. The effects increased by increasing the intraocular pressure. The reduction in volume of the vascular system represents a negative feedback mechanism. This is included in the "Intraocular vascular system" in Fig. 2.

A few minutes after the elevation of the intraocular pressure the narrowing of the vessels was followed by a slight dilation of some venules and some of the coarser capillaries as part of a vascular recovery phase.

(2) Vascular positive feedback mechanism. — The choroidal veins were especially sensitive to increased intraocular pressure at the point where they bend around the scleral margin just inside the trans scleral opening to emerge into the vortex vein (Fig. 3). Significant depression, or flat



Fig 8

Case 6 53 vision 0 2 Angiogram showing defects of the pigment epithelium in particular in the peri macular area

terminal stage of the macular process With increasing age all patients are likely to exhibit similar features

Fig 8 shows another type of pigment epithelial destruction The macular region is less severely affected but the angiograms reveal extensive pigment changes in the perimacular area

Certain facts concerning the circulation in retinoschisis have been clarified with the aid of fluorescein angiography Patient No 7 with a visual acuity of finger counting 3 m shows the disease in severe form The lower temporal vein is ramified (Fig 9A) with one branch running into the retinal veil and another continuing in the temporal direction Thirteen seconds after the injection of fluorescein the temporal branch is fluorescent (Fig 9B) The blood coming from below from the veil, is not fluorescent and forms a non fluorescent streak in the main trunk This

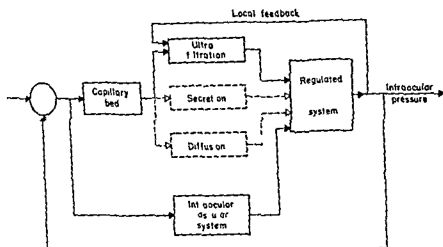


Fig 2

Intraocular feedback mechanisms The processes of ultrafiltration secretion and diffusion (across the blood aqueous barrier) represent the formation of aqueous humor The processes of secretion and diffusion are less known and they are therefore indicated by dotted lines For further details see text

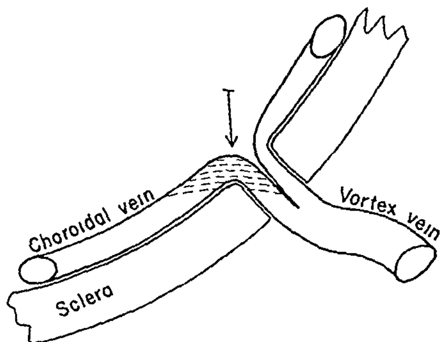


Fig 3

Schematic drawing of a vortex centre with the pressure-sensitive venous point (arrow) The dotted lines indicate the depression of the choroidal vein at the scleral opening



C



A



B

Fig 7

Case 5 68 *vision finger counting* 3 5m *A* Localized macular process *B* Stronger fluorescence temporally *C* Large choroidal (?) blood vessel the strongest fluorescence is seen nasally

tening, of the vein on its convex side could be observed even following an increase of 1 mm Hg of the intraocular pressure The degree of depression increased with increasing intraocular pressure until complete cessation of the blood flow at an increase of 5 mm Hg for the smallest veins and 20–50 mm Hg for larger ones Although the total blood flow through the pressure sensitive venous points was reduced, the blood *proximal* to these points, *i e*, in the vein through the trans scleral opening into the vortex vein, streamed faster than before This is the first direct demonstration of "the vascular waterfall phenomenon" previously postulated in the lung by Permutt, Bromberger Barnea and Bane (1962) The reduced outflow of blood from the choroidal veins tends to increase the intraocular pressure through their increase in volume, representing a vascular positive feedback mechanism This process is included in the "Intraocular vascular system" in Fig 2

The elevated venous pressure is likely reflected in the capillaries and thus secondarily influences the aqueous formation by increasing the ultrafiltration rate

Vascular recovery change was also observed at the pressure sensitive points

(3) *Capillary bed feedback mechanism* — A conspicuous phenomenon seen on increased intraocular pressure was the markedly reduced blood flow through the capillary bed, as judged from the slower speed of the blood corpuscles and the reduced vessel diameter The phenomenon was present after an increase of 4–5 mm Hg At this pressure level (19–20 mm Hg) some of the capillaries were completely empty of blood, and this vascular effect increased by increasing the intraocular pressure This decreased area of the capillary wall permeable to fluids reduces the aqueous humor formation The effect tends to stabilize the intraocular pressure and may be considered as a negative feedback mechanism (Fig 2, "Capillary bed")

Comments

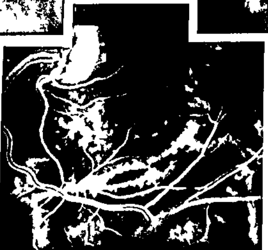
The intraocular vascular negative and positive feedback mechanisms influence the intraocular volume and consequently contribute to the acute change of the intraocular pressure The increased vascular resistance at the pressure-sensitive points at the venous outflow, i e, the waterfall phenomenon, operates concomitant with the increased vascular resistance at the inflow in the ciliary processes It thus help to maintain the circulation in the choroidal veins under increased intra ocular pressure This security measure is brought into play at intraocular pressure rises as low as 1 mm Hg



C



A



B

Fig 9

Case 7 15 vision finger counting 3m *A* The temporal lower vein sends a branch downwards into the veil (arrow) *B* Non fluorescent blood comes from the veil *C* At the end of the venous phase the same phenomenon is seen as in *B*

The capillary bed feedback mechanism results in a diminished aqueous humor formation and is thus included in the pseudofacility of Barany The reduced ultrafiltration rate due to the increased intraocular pressure (also part of the pseudofacility) is represented by the local negative feedback (Fig 2)

It should be noted that the vascular effects in the ciliary processes by sympathetic nerve stimulation is almost identical to that seen on increased intraocular pressure

All these intraocular feedback mechanisms except the positive one, take part in a common process by which changes in intraocular pressure are minimized

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streak can be followed as far as the papilla The same phenomenon also appears in the last picture (Fig 9C), after 23 sec, although the venous phase approaches its termination

The course is similar in case 8 In Fig 10A the lower temporal main trunk is seen to continue into the veil and a narrower branch continues peripherally of the veil over the choroid, which is atrophic In Fig 10B the vein coming from below is fluorescent, but centrally the blood stream is heterogeneous Obviously there is non fluorescent blood coming from the veil The nasal main trunk is conspicuous and filled with homogeneously fluorescent blood Throughout the course of angiography the blood stream from the veil remains unchanged (Fig 10C), although the fluorescence in the other veins decreases These observations show that the circulation in the veil is impaired Whether the impairment is the cause or the result of progression of the pathological process remains an open question

The last series of pictures moreover, exhibits pigment epithelial injuries both centrally and peripherally of the vascular veil In Fig 10C the large vessels of the choroid are therefore discernible peripherally They seem to be normal, and since the choriocapillaris shows normal fluorescence, there is no evidence of any significant involvement of this area of the choroid

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Head *R Tornquist, M D*

EXPERIENCES WITH RETINAL CYROSURGERY

By

Ragnar Tornquist

The first trials of freezing techniques in the surgery of retinal detachment (Bietti 1934, Deutschmann 1935, Cavara 1935, Veil and Dolfuss 1939) did not lead to general acceptance of the method The main reason was that diathermy was more convenient to use (Bietti 1968)

About five years have now elapsed since the renaissance of cryo surgery through Kelman and Cooper (1963) and Lincoff, McLean and Nano (1964) and it may be of interest to consider its value in retinal surgery The technical problems, even with new and improved instru ments, have been considerable From experimental and clinical studies, information has been collected concerning the biological effects of cryo techniques as a basis for comparison with diathermy

At the Eye Clinic in Örebo 800 eyes have been treated for retinal detachment and related conditions between 1 2 1961 and 30 3 1969 Cryosurgery was performed on 272 patients (290 eyes) The total number of such operations was 366

In the majority of operations the Kelman Retinal Cryopexie instru ment (Frigitronics) was used Cooling is produced by Freon fluid which is expanded into a vacuum through a microvalve Warming is achieved by passing warm Freon fluid through the tip of the instrument, and the process is monitored by a temperature gauge The instrument functions well if it is used by an experienced operator Drift disturbances from leakage at the joints, breakage of leads in the electric temperature registration and mechanical faults in the microvalve can occur and require repair by the manufacturer

During the last year other apparatuses were used Amoils Cryo Pencil unit (Keeler) and the Cryal apparatus (L air Liquide) Both instruments are well suited to retinal cryosurgery and have some advantages but also some disadvantages compared to the Frigitronics instrument The author's experiences with these instruments are rather limited at present

The results in the cases treated by cryotherapy are shown in Table I In the total series healing was achieved in 84 per cent The observation

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time is between 3 months and 3 years However, assessment of the results, especially if comparisons are made is not possible without knowledge of the composition of the material, the indications for treatment and the types of operation

Table 1
Retinal cryosurgery in Örebro
1 6 66–31 3 69

	Number of eyes Total	Cured
A No previous retinal surgery		
Predetachment	66	64*
Retinal detachment	181	142**
	247	206
B Reoperation	43	38
	290	244 (84 per cent)

* Additional photocoagulation in 16 eyes
** Additional photocoagulation in 9 eyes

Since 1961 the patients at the Örebro clinic have been recruited from other regions of the country to an increasing extent (Fig 1) Since there is only one eye clinic in the county of Örebro the group of patients who come from this area can be considered as representative of the population, while those patients who are admitted to the clinic from other areas are mostly selected cases of a complicated nature

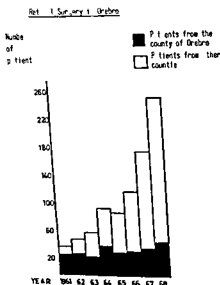


Fig 1

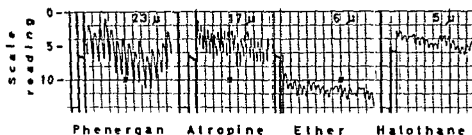


Fig 9
Influence of Phenergan atropine ether and Halothane N O O on corneal indentation pulse amplitudes Sensitivity settings 20 and 2 mV per paper division

was initiated a marked decrease in both blood pressure and intraocular pressure were noted (Fig 8) The corneal indentation pulse amplitudes did however only yield a rather slight corresponding decrease

Comment

The present study demonstrates a marked and significant decrease in corneal indentation pulse amplitudes initiated either by sleep following Seconal or Thiopentone administration or by ether or Halothane general anesthesia This decrease of corneal pulse amplitudes does not seem to be caused by a change in blood pressure as the blood pressure was unchanged in many of the cases studied

During general anesthesia a minor but *significant* decrease of the intraocular pressure was noted To a small extent this decrease of intraocular pressure may participate in explaining the decrease in corneal indentation pulse amplitudes as a slight reduction in corneal pulse amplitudes occurs with a decrease in intraocular pressure (*Hørven* 1970 b) As judged by the previously presented data (*Hørven* 1970 b) the decrease in corneal indentation pulse amplitudes which exists between the eye tension level 5 0 and 6 5 as measured with the 5 5 g plunger weight should be less than 10 % Accordingly the main cause of the marked decrease observed in corneal indentation pulse amplitudes following Seconal or Thiopentone administration and during general anesthesia is not properly explained by the slight reduction in intraocular pressure and should need some further discussion

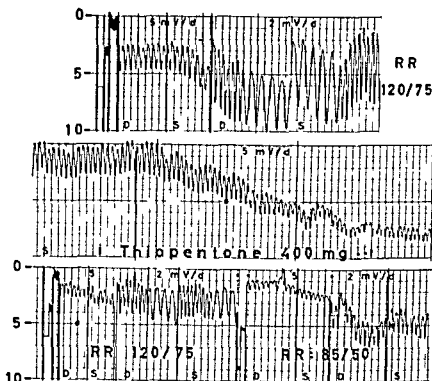


Fig 8

Influence by intravenous Thiopentone injection (midle) normal Halothane N_2O O_2 anesthesia (bottom left) and very deep Halothane N_2O O_2 anesthesia (bottom right) on blood pressure and corneal indentation pulse amplitudes Sensitivity settings 10 5 and 2 mV per paper division

As the corneal pulse primarily reflects the pulsesynchronous change in ocular volume initiated by the excess of blood entering the eye in systole a decrease in corneal pulse amplitude reflects a corresponding decrease in the excess of blood which enters the eye in systole Theoretically this decrease may be caused either by a reduction in ocular blood supply or by a change from pulsatile towards non pulsatile flow or both A strong indication that a decrease in ocular blood supply really is initiated by general anesthesia was offered by *McGowan* (1967) who reports a case of giant cell arteritis which turned amaurotic during general anesthesia A similar case was recently observed in Oslo City Hospital (*Bergaust* 1968) in this case the diagnosis of giant cell arteritis was verified after general anesthesia was given with amaurosis as a result Most probably these eyes which yielded no symptoms prior to general anesthesia still had a reduced ocular blood supply as a consequence of giant cell arteritis lesions in their ophthalmic arteries a possibility which have been proved valid in other cases of

The indications for treatment have remained unchanged since 1961 To a great extent it has been the aim to operate also on cases with a poor prognosis and re operations have been performed so long as there has been any chance of improvement In about 5 per cent of the patients admitted for assessment surgery has not been performed Retinal cysts comprise the majority of such cases where surgery has been considered contraindicated In a few cases the prognosis has been regarded as hopeless or contra indications of a general nature have prevented surgery

The method for producing the adhesive chorio retinitis was changed in June 1966, when diathermy was replaced by cryotherapy However, during a transition period diathermy was used to a certain extent, chiefly in those cases for which this method had been used previously (Table II) At about the same time treatment by trans conjunctival cryopexy was instituted for conditions which would previously have been photocoagulated (for example, retinal tears near the ora serrata)

Table 2

Methods of retinopexy Örebro 1961–1969

Year	Number of operations			
	Photocoagulation	Diathermy	Cryopexy	Total
1961	19	32		51
1962	32	41		73
1963	24	52		76
1964	36	73		109
1965	27	51		78
1966	35	59	38	132
1967	31	47	89	167
1968	36	36	191	263
1969–30 3	3	0	48	51
Total	243	391	366	1 000

The technique for producing chorio retinal contact at operation has remained constant If a retinal elevation was present scleral buckling was usually performed with a silicone plomb according to the principle of Custodis Evacuation of subretinal fluid was generally avoided If this was done it was often combined with injection of air Only in particularly complicated cases encircling procedures were performed In some cases the silver ball method of Rosengren (modified by Kloti) and vitreous implantation were performed

For comparison between the cryo and diathermy methods cases with manifest retinal detachment not previously operated on were selected Prognostically unfavourable cases were collected in a group ('complic'), which included the following types of cases

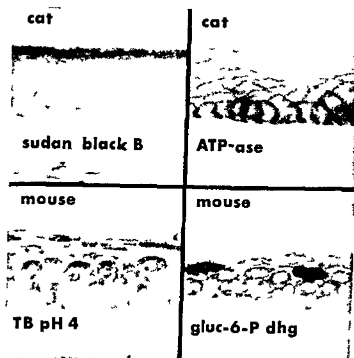


Fig 2

Localization of lipids (sudan black B), ATPase RNA basophilia (Toluidine blue pH 4) and glucose 6 phosphate dehydrogenase in the corneal epithelium

Table 2

Effect of some ions and pharmaca on the activity of acid phosphatase and ATPase in the corneal epithelium

	Acid phosphatase monkey rabbit (mM/l)	ATPase monkey (mM/l)
Mn^{++}	activates (10 0)	activates (10 0)
Mg^{++}	activates (10 0)	activates (6 0 54 0)
Cu^{++}	inhibits§ (1 0 10 0)	inhibits* (5 0 10 0)
F^{-}	inhibits§ (10 0)	inhibits* (10 0)
g strophantin	no effect§ (0 1 1 0)	no effect* (0 1 1 0)
acetazolamide	no effect§ (1 0)	no effect* (0 5)
atropine sulphate	no effect§ (1 0)	no effect* (10 0)
pilocarpine chloride	no effect§ (1 0)	no effect* (10 0)
cocaine chloride	no effect§ (1 0)	no effect* (10 0)
physostigmine salicylate	no effect§ (1 0)	no effect* (5 0)

Any effect estimated by comparing sections incubated with and without the substance examined

§ Mn^{++} (10 0 mM/l) added as activator

* Mg^{++} (10 0 mM/l) added as activator

1 No tears visible
2 Giant tears, multiple holes in more than one quadrant
3 Total detachment
4 Preretinal traction
5 Examination difficult (non cooperative patient, cloudy media posterior synechia etc)

The remaining cases composed a more homogenous group (simple ') with a better prognosis The comparison between the diathermy and cryo methods in the two groups is shown in Table III The differences between the two methods are not significant

Table 3
Cases of retinal detachment with no previous retinal surgery

Method	Retinal detachment	Number of eyes Total	Cured	
Diathermy	"simple	100	89	(89%)
	complic	161	109	(68%)
	total	261	198	(76%)
Cryopexy	simple	103	95	(92 5%)
	complic	78	47	(60/)
	total	181	142	(78 5%)

The frequency of complications with cryotherapy is probably low Insufficient chorio retinal adhesion is not to be feared according to experimental studies Assessment of the effect is made at operation, either with each application (treatment of small areas well seen ophthalmo copically) or after single test application whereat temperature and time are noted Freezing is stopped when the choroid becomes grey white that is when the choroidal temperature falls below freezing point If retina is brought into contact with the wall of the globe by pressure with the instrument a white discoloration of the retina is seen more clearly Clinical experience shows that in spite of this control poor adherence is sometimes obtained postoperatively This happened in 14 cases and re-operation was necessary Experience shows that especially with choroidal atrophy one should apply more powerful freezing or combine the procedure with photocoagulation

Retinal and choroidal haemorrhage can occur with cryotherapy if when the instrument is frozen onto the sclera it is removed quickly without defreezing Damage to tissues is then produced and usually small capillary haemorrhages result With proper care however this risk is probably small The walls of the larger vessels are not damaged by



Fig 3

pH dependence of phosphatase activity in the superficial cells of the corneal epithelium The reaction intensity is given as the *reciprocal of the time in minutes to positive* reaction

while in cat and pig only the basally localized activity was found The alkaline phosphatase reaction took place at p*H 8 10 It* was *markedly* weaker at pH 7 and had disappeared at pH 6 In animals showing acid as well as alkaline phosphatase superficially in the epithelium two reaction maxima could be observed (Fig 3) showing the presence of two different enzymes

In all the species investigated glycogen and the enzymes from the oxidative metabolism could be demonstrated(5) Enzymes from the pentose shunt especially glucose 6-phosphate dehydrogenase (NADP) varied in intensity from one cell to the next Cells with high activity (Fig 2) also showed a high content of RNA This suggests a protein synthesis but the particular function of these cells is unknown Mitoses are only rarely seen above the basal layer and the cells do not differ morphologically from the surrounding cells

The cells appearing morphologically different in sections have never been observed to differ metabolically from the surrounding cells

Physiological studies

Enzymatic differences are present among animal species even among the frequently used experimental animals as rabbit rat, cat and monkey Also in other respects there seem to be functional differences An electrical

freezing and no haemorrhage from these has been observed However, a hyperaemia of the treated areas develops some minutes after treatment This may be the reason for the accidental haemorrhage in association with puncture through a previously frozen area (Bietti 1968) In our material intra and sub-retinal haemorrhage has occurred in 8 cases in association with the release of subretinal fluid after cryotherapy It is advisable to refrain from this procedure, and if possible the puncture should be per formed within areas which have not been frozen

The advantages of cryotherapy thus do not comprise better and more certain healing between the retina and the wall of the globe Indeed, in some cases the adherence is weaker But the risks of serious complications are probably less than with diathermy Those relatively common com pleting operations which are probably unavoidable in retinal surgery (because of poor retino choroidal contact, weak adherence, etc) are made considerably simpler because re operation is easier to perform and not usually associated with greater risks than the primary operation The intact scleral wall also makes erosion of the sclera with encircling suture according to Arruga less likely In only one case out of 44 when cryo therapy was applied with an encircling procedure has a small erosion been seen

At the Orebro clinic we feel that at the moment we are able to dispense with the diathermy operation for retinal surgery cases The importance of good postoperative chorio retinal contact is probably greater than with the diathermy operation and the surveillance of the development of the chorio retinal adherence around the retinal hole must be more careful Probably it is necessary to complement the operation with photocoagu lation to a greater extent The essential advantage is more *lenient treat* ment of the eye It seems to be a progress in the development of retinal surgery with its trend towards more complicated and traumatic opera tions

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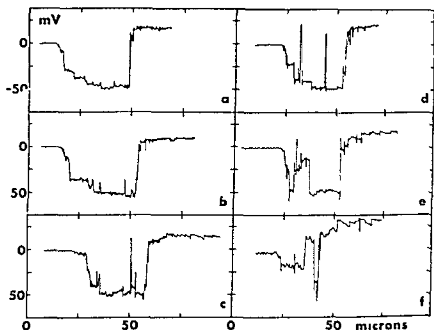


Fig 4

Typical potential recordings from penetrations or rabbit corneas Abscissa position of microelectrode Ordinate potential in mV The time of penetration is about 30 secs The electrode is moved from left to right In a, b and c the transcorneal hydrostatic pressure was 18 mm Hg in d 29 mm Hg and in e and f 37 mm Hg In experiments e and f the endothelium was scraped off

potential difference of 15–20 mV exists across the rabbit corneal epithelium, with the outside negative in relation to the stroma (4) This potential difference has been demonstrated in the ox, but not in man or cat

Intracellular potentials The elecrical potential profile through the epithelium was studied by means of microelectrodes with a tip diameter of 0 25μ(6) Negative intracellular potentials of about 40–50 mV were recorded in all experiments on rabbit, cat, ox, rat, and dog corneas Only rabbit and cat were subjected to closer studies (Figs 4 & 5) The fall in potential in the surface of the epithelium often occurred over a distance of 5–10μ, after which no regular changes were seen until a sudden change in positive direction occurred at the basement membrane In the rabbit an overall transepithelial potential of about 15 mV with inside positive was found (Fig 4) In the cat no transepithelial potential could be demonstrated

In about 50 per cent of all penetrations positively directed peaks were recorded within the epithelium The peaks reached the level of the inside potential, but this was never exceeded The number and the width of the peaks increased when the transcorneal hydrostatic pressure was increased

Discussion

B Rosengren (Gothenburg)

In the nineteenthirties one tabulated three conditions which had to be fulfilled if one was to expect healing of a detached retina according to a principle of Gonin

1 The operation had to be performed at the site of the rupture or ruptures The question of identification was therefore very important By practise an ophthalmoscopic examination could reveal about 95 % of the retinal holes The reason for an unsuccessful outcome could therefore rarely be blamed on a failure to identify the ruptures

2 Coagulation had to be performed around the rupture By the introduction of diathermy in 1930 this condition was easily fulfilled

3 A physical contact between the retina and the choroid had to be achieved by some means in order to expect healing This was a very difficult problem Before the introduction of methods which had a clear and sound theoretical basis the success rates were below 50 % In my own case the outcome of operations on 29 patients in the years 1933–36 resulted in a success rate of 45%

In 1936 I started to examine the operated eyes (with an ophthalmoscope) only a few days after the operation and in some cases I noticed that the detachment was very high I tried to inject air into the vitreous body in order to produce a pressure which could approximate the retina to the choroid in the region of the rupture This procedure resulted in an immediate increase of the success rate to 78% and this figure was more or less constant from 1936–1954 During these years this method was used as routine at eye-clinic in Goteborg

The buckling operations which were introduced by Lindener in 1933 had in the beginning a very uncertain theoretical basis and the results of the operations were very difficult to evaluate The rationale behind the operation was to decrease the size of the scleral to accommodate the detached retina The method was improved by Shapland who in 1951 produced a buckle by lamellar resection of the sclera In 1949 Custodis demonstrated a spontaneous regression of the detachment by placing the buckle exactly adjacent to the rupture This important observation has made this method the one of choice to obtain contact between the detached layers during the healing period. By using this procedure the usual success rate is in the order of 80–85% If the contact operations were to be given up one would expect to return to the old success rate figures of less than 50

The question in our context is however what influence the new cryotherapy will have on the success rate It is evident that this method is less destructive than ordinary electrodiathermy One will therefore expect less retinal damage in the central areas and a better visual acuity in the successful cases In addition it causes very little scleral damage and this makes a reoperation easier

Is the electrodiathermy coagulation not realistic therapeutical alternative nowadays? The question cannot be answered at present If an improvement in the diathermy method could produce as undestructive and uniform lesions as seen by the cryotherapy method it would through its simple construction offer an alternative

Finally I would like to congratulate Docent Tornquist with his very high success rates The thorough and very critical evaluation of the cases give these figures an additional value

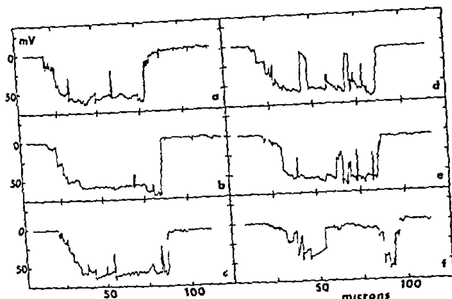


Fig 5

A sequence of penetrations from a cat cornea a b and c are recordings at 15 min intervals Transcorneal hydrostatic pressure 20 mm Hg In d e and f the transcorneal hydrostatic pressure was 45 mm Hg The pressure had been maintained for 30 min before the recordings were made at 15 min intervals

This procedure is known to dilate the intercellular spaces, and it is probable that the peaks represent intercellular spaces in direct communication with the inside

Comments

The corneal epithelium is very regular, showing only small morphological species variations In the surface cells lipids may be demonstrated probably originating from the Meibomian glands and taken up by the cells by pinocytosis

Cells of different morphology are seen in the epithelium but demonstration of enzymatic differences between morphologically different cells has proved unsuccessful Tissue culture studies did not show several types of cells As the morphological differences could always be explained stereometrically when the orientation of the sections was carefully considered it must be concluded that proofs of the existence of several functionally different cell systems in the epithelium have been given neither in literature nor in the present studies

The transepithelial potential demonstrated in the rabbit is a function of the entire epithelial layer, whereas the energy requiring processes probably occur as ion transports across the surface membrane of the

freezing and no haemorrhage from these has been observed However, a hyperaemia of the treated areas develops some minutes after treatment This may be the reason for the accidental haemorrhage in association with puncture through a previously frozen area (Bietti 1968) In our material intra- and sub retinal haemorrhage has occurred in 8 cases in association with the release of subretinal fluid after cryotherapy It is advisable to refrain from this procedure, and if possible the puncture should be per formed within areas which have not been frozen

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individual cells The "box profile" of the intra epithelial potentials with approximately the same negative level in all cells suggest that these are electrical in parallel It is still unknown how the functions of the cells are integrated The ionic composition of the bathing fluids influence the potentials The surface potential is sensitive to sodium and anions, the potential change at the basement membrane is potassium sensitive Species differences in the composition of the tears and the interfibrillar fluid of the stroma may explain why no transepithelial potentials have been demonstrated in the cat and the human cornea (4 6) Another explanation is that no potential difference is maintained *in vivo* It is, however, difficult to demonstrate the lack of a potential

If there are species differences in the existence of a transepthelial potential, it is tempting to correlate these with species differences in enzyme content In this respect the superficially localized alkaline phosphatase is interesting In the rabbit and the ox both transepithelial potential and phosphatase activity are found, in man and cat both are lacking Further studies on this possible correlation are needed It must be concluded that whereas negative intracellular potentials appear to be a general biological phenomenon, it is still unknown if a transepithelial potential is of more general occurrence and should be considered in the maintenance of the normal functions of the cornea

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Acta Ophthalmologica Vol 48 1970

SOME COMPARATIVE STUDIES ON THE MAMMALIAN CORNEAL EPITHELIUM

By

Niels Ehlers

The corneal epithelium has been the object of many investigations but in spite of this, problems of *structural as well as functional nature remain* Some of these however are only apparent originating in the use of different techniques *and of different animal species* This paper presents the results of some comparative studies ,parts of which have been reported elsewhere (see references)

Histological studies

Table I shows the mammals included in the studies The thickness of the epithelium and the number of cell layers vary from one species to the next The epithelium is generally thinnest in the centre of the cornea, and thickness and number of cell layers increase towards the limbus Compared with the difference in size of several of the species investigated the thickness and the number of cell layers show little variation

Morphology The cells of the epithelium are described as being in three layers a basal an intermediary and a superficial layer The size of the superficial and intermediary layers varies In the ox the intermediary layer is *the largest In whale and seal* an extremely highly developed superficial layer with well over ten layers of flattened cells is found while the intermediary layer *comprises only a few layers of cells The many superficial* cells are probably a protection against the hypertonic sea water

In all species examined the epithelium is stratified squamous and non keratinized In older literature it is mentioned that the epithelium is keratinized in the whale During the present investigations(5) it has not proved possible to demonstrate keratohyalin granules in the epithelium of the whale nor have the special stainings (mercury orange) given support to the supposition of keratin formation

In the literature descriptions of various kinds of cells in the epithelium are found Apparently each author has observed a new kind of cells It is

Acta Ophthalmologica Vol 48 1970

CHANGES IN THE MOLECULAR MORPHOLOGY OF THE VITREOUS AFTER INTRAOCULAR SURGERY

By

Sven Österlin

The hyaluronic acid concentration in the vitreous of aphakic eyes is considerably lower than in the corresponding phakic eyes The implications of this finding in relation to the importance of the hyaluronic acid in the molecular morphology of the vitreous and to the post operative changes in the vitreous following uneventful intracapsular lens extraction is discussed

To be published in final form in the Transactions of the XIX World Congress of Ophthalmology

Acta Ophthalmologica Vol 48 1970

DEAD, DEGENERATE, AND LIVING CELLS IN CONJUNCTIVAL FLUID AND MUCOUS THREAD

By

M S Norn

Published in *Acta Ophthalmologica* 47, (1969), 1102–1115

ON TRANSPLANTATION OF CORNEA AND PERILIMBAL SCLERA IN RABBITS

By

J. Hetland-Eriksen

To be published in *Acta Ophthalmologica*

Discussion

H. Valebjorg (Oslo)

This is the age of transplantations, and I would like to mention a case where acrylic has been used. This plastic causes very little tissue irritation. The first illustration shows the acrylic window placed in the sclera just behind the ciliary body (Valebjorg 1963). As result of the operation some blood corpuscles appeared just behind the lens, and these corpuscles were later organized. The conjunctiva from the palpebra and the bulbus encircled the fenestration and resulted in complete apposition to the window. The eye was pale and free from reactions. One could demonstrate a normal pupillary reaction and I had the impression that the rabbit had a normal vision on this eye. A year after the operation an acute inflammation of the bulbus appeared (injury ?). The intraocular condition, however, showed no changes.

The illustration demonstrates the fenestration of the bulbus.

Ref. Valebjorg H. Fenestration bulbi posterior. A method for the investigation of the function of ciliary body and adjacent organs in experimental animals.
A preliminary report. Acta Ophthal. 1963. *41*, 313–316.



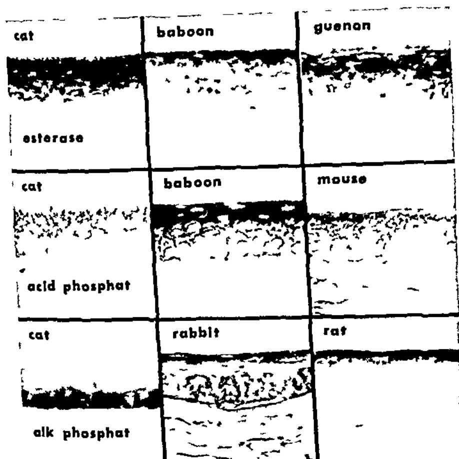


Fig 1

Histochemical enzyme reactions in the corneal epithelium Naphthol As-acetate esterase and acid naphthol AsBi phosphatase is localized mainly to the superficial cells Alkaline naphthol AsBi phosphatase shows species variations in localization

preted as a pinocytosis of lipids originating from the Meibomian glands (2) ATPase was found to be localized in the cell membranes with the exception of those facing the basement membrane(5) (Fig 2) This enzyme is often correlated to active membrane transport The general occurrence of acid phosphatase and of ATPase gave rise to an examination of the effect of certain ions and drugs upon the enzyme activity The results are shown in Table II

Alkaline phosphatase showed variations between the individual species(3 5) (Fig 1) In man and monkey no reaction occurred In ox, dog rabbit guinea pig rat and mouse a superficial reaction was found In dog and rabbit besides the superficial localization a basal activity was found

GENERAL MEETING

G on Bahr Report on N O L R
The accounts were submitted The activities will continue as hitherto

Holger Ehlers

Report on Acta Ophthalmologica

Since my last report in Copenhagen 1967 the Acta has shown a steady progre s

Volume 45 1967 and volume 46, 1968 comprised 884 and 1 277 printed pages respectively During these two years nine supplementa were issued

It should be noted that the Acta from volume 47, 1969 has been printed on coated paper more fit for reproduction of fine details

The subscription rate is 150 D Kr It is felt that Acta Ophthalmologica is still an inexpensive periodical considering quality, quantity and not forgetting the supplementa which in most cases are Scandinavian doctorate theses

About one third of the whole issue is distributed in Scandinavia two thirds all over the world

Election of new Editor in Chief of Acta Ophthalmologica

Professor Holger Ehlers retires as Chief Editor of Acta Ophthalmologica at the end of 1969

Professor Poul Brændstrup was elected as new Editor in Chief from January 1970

Table 1
Thickness and number of cell layers of the corneal epithelium

Animal species	Number of eyes	Epithelial thickness	Number of cell layers
man	8	30–40	5–7
baboon	6	35–45	5–7
guenon	14	30–40	5–7
vervet monkey	4	35–45	5–7
pig	9	50–70	6–9
cat	8	35–50	6–8
ox	6	90–120	10–15
dog	7	60–80	8–10
rabbit	9	30–40	5–7
guinea pig	14	30–40	5–7
rat	16	25–35	4–6
mouse	10	20–30	3–5
seal	4	60–90	10–15
blue whale	3	100–130	12–18
sperm whale	1	80–120	12–16
porpoise	4	40–60	10–14

The thickness in μ and the number of cell layers refer to the central cornea The thickness was measured on formalin or formol calcium fixed sections cut perpendicular to the surface This fixation gives only a minor shrinkage as compared with fresh frozen sections which were unfortunately not available for all species studied

remarkable that there exists a large number of electron microscopic examinations of the corneal epithelium which fail to mention the presence of several kinds of cells In the present investigations (5), the existence of morphologically different cells have been verified This, however, cannot in itself be considered proof of the existence of several kinds of cells, perhaps functionally different as the morphology observed may be explained purely stereometrically and may very well represent the differentiation of the normal cell

During investigations of epithelial cells in tissue culture (1) with special reference to the presence of several kinds of cells in the epithelium, continuous photographing unveiled transformations between the various morphological types, and it was assumed that they represent states of the life cycle of the cells

Cytochemistry In all the species investigated a strong, mainly superficially localized reaction for naphthol As esterase and acid phosphatase (naphthol AsBı phosphate) was found(2 5) (Fig 1) These two enzymes may be correlated to the occurrence of lipids in the surface of the epithelium of all species examined (Fig 2) The function of these enzymes has been inter-



Presentation of the K. K. K. Lundsgaard Medal

Professor Holger Ehlers presented the K. K. K. Lundsgaard Medal in gold to professor *Arno Oksala*, Turku, Finland, for his outstanding and progressive work in ultrasonography in ophthalmology. This activities cover methods, fundamental aspects and clinical application. Scandinavian ophthalmology and the Acta Ophthalmologica profited greatly from professor Oksala's steady and continued studies.

Dr. Kristjan Sveinsson invited to the next *Nordic Meeting of Ophthalmolgists* in Iceland in 1971.

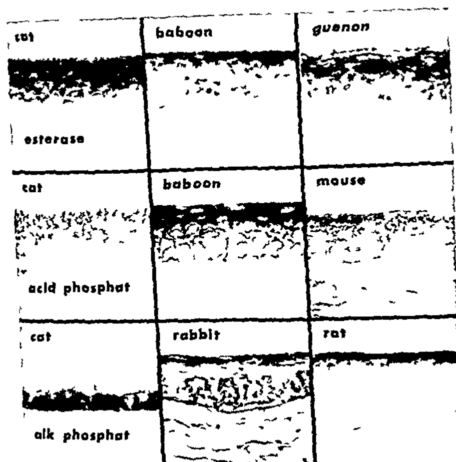


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Denmark
Brunte, Else, Herning
Bruun Jensen, Jørgen, Slagelse
Brændstrup Johanne Marie København
Brændstrup Poul København
Damgaard Jensen Ehlert, Aarhus
Dreisler, Knud Holbæk
Dreyer Viggo, København
Edmund, Jens, København
Ehlers Holger, København
Ehlers Nils Aarhus
Eldrup Jørgensen Poul, København
Fabricius Agnete, København
Glissov, Bent Næstved
Godtfredsen Erik, Hellerup
Heidensleben Erik Rungsted Kyst
Jensen Jens Sønderborg
Jensen Ove Aksel København
Jensen Viggo A Aarhus
Kesing Svend Vedel København
Kjeldsen Mogens H Vejle
Kjer Poul Hellerup
Knudtzon Karsten Hellerup
Kristensen Preben Thisted
Larsen Hans Walther, Hellerup
Lawaetz Børge København
Lorentzen Svend Erik København
Madsen Poul Henry Odense
Marner Else København
Møller P M Odense
Møller Nielsen Niels Ole Holstebro
Norn Mogens Stig Vanløse
Ohrt, Vagn, Aalborg
Pouplier, Gunnar Svendborg
Reeh Pedersen Lisbeth, København
Riise Dag København
Riise Ruth København
Rud Erik, Frederikshavn
Seedorff Hans Henrik København
Skydsgaard, *Henning København*
Svane Knudsen, Poul Kolding
Vedel Jensen Niels Hjørring
Vesterdal Elise, København
Westerlund Erik Nykøbing Fl

Finland
Elenius Valter Åbo
Ennevaara Kai Kajana
Forsius Henrik Uleåborg
Heikkila *Heikki Antti Tammerfors*
Karo Terttu Åbo
Krause Ulf, Uleåborg
Kyrki, Liisu Uleåborg
Lehtonen Jarmo Lahtis
Marjanen Sinikka, Åbo
Mustonen Eila Uleåborg
Suvanto Erkki Björneborg
Vasama Ritva Tammerfors
Voipio Hannu Helsingfors

Iceland
Sveinsson, Kristjan, Reykjavik

this disease (*Horven* 1970 c) The reduced blood supply yielded presumably sufficient nourishment of the eyes until general anesthesia initiated a further decrease in ocular blood supply with amaurosis as a result As a consequence of this interpretation it is advisable for patients suffering from giant cell arteritis to have a dynamic tonometry examination performed prior to accepting surgery under general anesthesia If this test demonstrates a decrease in corneal pulse amplitudes in eyes with useful vision the general anesthesia should if possible be avoided

The present demonstration of a decrease in corneal pulse amplitudes initiated by sleep following Seconal or Thiopentone administration may also have a bearing in explaining the point stressed by *Meadows* (1968) that clinically the blindness in giant cell arteritis very often is noted in the morning following a good nights sleep

As mentioned above the excess of blood entering the eye in systole will initiate a change in intraocular pressure which in man and animals may be recorded by various tonometry methods of which dynamic tonometry is preferred by the authors and in animals by a direct approach by application of a pressure transducer to a canulated eye *Laurence & Schlegel* (1966) demonstrated in Urethane anesthetized rabbits a pulsesynchronous change in intraocular pressure of 0 2 mm Hg (normotensive eyes) and 1 5 2 3 mm Hg (hypertensive eyes) Similar results were presented in Nembutal anesthetized rabbits by *Bynke* (1968) The previously mentioned preliminary experiment in Nembutal anesthetized rabbits performed by one of us (I H) yielded results confirmative with these observations Thus the pulsesynchronous change in mm Hg intraocular pressure reported from anesthetized rabbits is only 15 30 % of the values obtained in non anesthetized human beings (*Horven* 1970 b) The values reported in rabbits are of the same order of magnitude however as the values obtained in man during general anesthesia Results concerning the pulsesynchronous change in intraocular pressure and volume obtained in rabbits during general anesthesia should therefore be accepted with a large part of skepticism As in man such results will probably not reflect the normal state of non anesthetized animals

Summary

The corneal indentation pulse was studied before following premedication and during general anesthesia in 24 patients (39 eyes) A significant decrease in intraocular pulsation was demonstrated following Seconal or Thiopentone administration and during ether or Halothane general anesthesia

The decrease in corneal pulse amplitudes observed during general anesthesia

most probably reflects a corresponding decrease in ocular blood supply Accordingly, if an emergency situation does not exist general anesthesia should not be accepted by patients suffering from giant cell arteritis unless a dynamic tonometry procedure have proved their ocular blood supply to be within normal levels

Acknowledgment

The skilful technical assistance of Mrs Gull Britt Huseby is gratefully acknowledged

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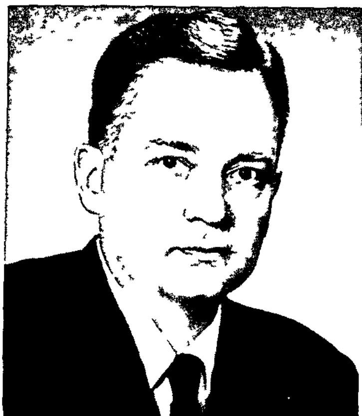
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Table 3
Age and sex distribution of 1882 patients subjected to routine tonometry

age	females	males	Total
35–44	127	250	377
45–54	217	365	582
55–64	134	272	406
65–74	97	212	309
75–84	91	97	188
≥ 85	9	11	20
Total	675	1207	1882

Patients with Applanation Values Below the Screening Level

In 1713 of the 1882 patients the applanation value found was below the screening level of 20 mm Hg in both eyes

As stated previously the applanation measurement formed part of a general eye examination This involved that in two patients glaucoma was suspected in spite of an applanation value below the screening level One of these patients was a man aged 75 whose optic discs were characterized as glaucoma suspicious but the suspicion could not be maintained after further examinations

In the case of the other patient – a woman aged 71 – anamnestic data were available which might be interpreted as rainbow rings around the light Gonioscopy revealed a narrow chamber angle whereas the results of the further examinations added no support to a diagnosis of glaucoma

According to the procedure chosen further examinations should also be offered to patients with a screening tension under 20 mm Hg if a difference of 4 mm Hg or more between the two eyes was recorded This was so in a total of eight patients (two males and six females) ranging in age from 42 to 85

However with a single exception the difference in tension could not be reproduced on control measurements The optic discs were normal and the visual field tests gave normal results in the six patients whose co operation was sufficient to permit satisfactory testing

In agreement with Davanger (1965) and Hollows & Graham (1966) the results of the present investigations thus suggest that recording of fairly great differences in *tension* between the two eyes in patients whose intra ocular

Holst Berg Tormod Oslo
Horven Ivar Oslo
Haarr Marius, Ålesund
Ihler Jon O Skien
Jensen Per Stavanger
Johansen, Otto Oslo
Klouman Otto Fredrik Kristiansand S
Kolstad Albert Oslo
Kristiansen Odd Julius Kongsvinger
Lager, Reidar, Tromsø
Larsen Jon Bergen
Loche, Ragnar, Tønsberg
Malling Birger Oslo
Midtbo Arne Drammen
Moi Ivar Sandefjord
Maartmann Moe, Erik, Hønefoss
Nicolaissen, Bjørn Oslo
Nordhagen Endre Hvalstad
Nyquist Bengt, Bergen
Odd Olaf Arendal
Odland Magnus Bergen
Omvik Per Bergen
Ringvold Amund Oslo
Rogge Albert J Bergen
Ross Reinulf Drammen
Roe Oluf Namsos
Sandvig Kaare Bærum
Sato Olav Oslo
Saugstad Arne Oslo
Schive Kirsti Bergen
Schjelderup Mathiesen Per Oslo
Sellevold Ole Jakob Arendal
Sokol Alf Bergen
Standal, Brynjulv Molde
Sunde, Olav Aga, Oslo
Syrdalen, Per, Oslo
Thomassen, Thore Lie, Oslo
Tjåland Johan Oslo
Torlei Knut, Bergen
Tveiten, Berge, Bergen
Tonjum, Knut Tonsberg
Uchermann, Albert Bergen
Udjus, Ludvig Bærum
Udnæs Ingar Oslo
Valebjorg Hallvard Oslo
Vallersnes Odd Haugesund
Wirsching Johan Chr Oslo
Wirsching, Ludvig sen , Kristiansand S
Wirsching Ludvig jr Kristiansand S
Waalen, Torbjorn Gjovik
Waaler, Paul Lillehammer
Ytteborg Jan Bekkestua
Aasved Henry, Bergen

Other countries

Gundersen Trygve Boston USA
Holm Knut U Brooklyn, New York, USA
Johnson Albin Raleigh N Carolina USA
Jorgensen, Donald R St Paul USA
Siemenstad L O Osceola Wisconsin USA
Worst Jan Gerben Frans Groningen, Holland

to an ophthalmic practice where as stated previously females have been found to attend in greater numbers than males

Further Examinations

Endeavours were thereafter made to either establish the diagnosis or refute the suspicion of glaucoma on the basis of the following lines laid down for diagnostic control examinations of the 169 screening *positive cases*

Control pressure measurements were arranged in ophthalmic practice within 1–3 months

Further examinations were thereafter carried *through as follows in* the Department of Ophthalmology *Centralsygehuset* Nykobing Falster

To these examinations were subjected patients with a screening pressure *of* 22 *mm Hg of at least one eye during* 3 *or* 4 days stay in hospital where they had a chance of renewed determinations of vision and refraction and of ophthalmoscopy In addition they were subjected to 24 hour pressure measurements (not less than four measurements between 7 a m and 8 p m.) scleral rigidity determination visual field measurement water provocative test priscol provocative test gonioscopy mydriasis test dark room test *and retina* photography

Patients with a screening pressure of 20–21 mm Hg were subjected to out *patient examination comprising determinations of vision* and refraction ophthalmoscopy visual field measurement gonioscopy water provocative test and pressure measurement preferably between 8 and 10 a m

However not all the 169 *patients could* have the diagnostic control examina*tions carried through on the* desired lines

Of the 169 patients 50 (29 6 per cent) failed to appear for the appointed control pressure measurements in ophthalmic practice and another eight had been admitted to hospital or been subjected to treatment immediately after the *screening*

Of the 89 patients with a screening pressure of 22 mm Hg or higher (see table 4) no more than 55 had examination carried through during stay in hospital As regards the 34 patients not admitted to hospital the main reasons for this were in some cases difficulty of making them consent to admission these *patients* having an unaffected vision and only slight eye *troubles (21* patients) while in others admission was desisted from owing to a poor general condition high age or inadequate co-operation (13 patients)

In addition to the above 55 patients *another seven with screening pressures* below 22 mm Hg were admitted Thus 62 patients were examined during *stay in hospital*

Of the remaining 107 patients 87 had out patient examination carried through in the ophthalmic unit while 20 did not attain to this stage Seven

Sweden

Algvere, Peep, Stockholm
Anjou, Ingvar, *Jonkoping*
Anseth, Arvid, Lund
Aurell, Elisabeth, Goteborg
von Bahr, Gunnar, Uppsala
Bergquist, Birgitta, Eskilstuna
Blix, Karin, Norrkoping
Blix, Magnus, Norrkoping
Bostrom-Smith, Inga-Lisa, Gavle
Bynke, Hans, Lund
Carlberg, Olof, Gavle
Dahlberg-Parrow, Ragna, Uppsala
Elg, Gosta, Kalmar
Enoksson, Paul, Stockholm
Ericson, Lennart, Uddevalla
Eriksson, Anna Stina, Boden
Ervaeus, Sigrid, Falun
Esklund, Alf, Solna
Granath, Ulla, Harnosand
Gronvall, Herman, Kristianstad
Hedbeck, Krister, Borås
Hjortzberg Nordlund, Ulla, Goteborg
Holm, Klas Krister, Falkoping
Holm, Stig, Goteborg
Holmberg, Åke, Stockholm
Jahnberg, Peder, Gavle
Kassman, Ture, Arvika
Kronning, Eric, Skelleftea
Laurent, *Ulla, Uppsala*
Magnusson, Loftur, Örebro
Malmquist, Folke, Goteborg
Mattsson, Ragnar, Goteborg
Nordlow, Waldemar, Vanersborg
Nylander, Ulf, Gavle
Olsson, Gunvor, Goteborg
Palm, Erik, Lund
Rehn, Nils O , Sodertalje
Rendahl, Carl Ilmari, Stockholm
Rexed, Ursula, Saltsjobaden
Ribbing, Kerstin, Linkoping
Rosengren, Bengt, Goteborg
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Sahlstrom, Ingvar, Stockholm
Sjogren, Henrik, Jonkoping
Suurkula, Juri, Goteborg
Tornquist, Ragnar, Örebro
Wadensten, Lars, Hudiksvall
Wolff, Herbert, Linkoping
Wranne, Ingrid, Uppsala
Wulfing, Bjorn, Stockholm
Österlin, Sven, Malmo
Österlind, Gote, Malmo

Norway

Askelund, Per, Trondheim
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Bergaust, Bjorn, Oslo
Bertelsen, Torstein, Bergen
Birkeland, Hanne, Oslo
Bjerke, Otto, Elverum
Blomskold, Gustav, Narvik
Bore, John, Haugesund
Braathen, Harald, Bergen
Braathen, *Sverre Johannes*, Stavanger
Bulie, Tore, Oslo
Christensen, Gunnar E , Fredrikstad
Davanger, Martin, Oslo
Egge, Kjell, Hamar
Eitrem, Egil, Tonsberg
Engesæter, Ludvig, Trondheim
Flage, Tor, Oslo
Foss, Bjorn, Oslo
Gjessing, Harald G A , Drammen
Granaas, Alf Hans, Kristiansand S
Gaarder, Ole, Oslo
Hansen, Egill, Oslo
Hetland Eriksen, Jens, Oslo
Holst, Hans J , Oslo
Holst, Johan Collett, Oslo

recorded in 47 patients (2 5 per cent) 25 mm Hg or higher and in 18 patients (0 96 per cent) 30 mm Hg or higher The highest pressure value measured was 54 mm Hg No patient under 45 years of age had a pressure of 30 mm Hg or higher recorded while only two under 45 had a screening value of 25 mm Hg or higher *In the groups with screening values of 25 mm Hg and of 30 mm* Hg 70 per cent were over 65 years of age

The recorded incidence (2 5 per cent) of pressure values of 25 mm Hg or higher is lower than the corresponding results reported in the literature from ophthalmic practices for patients over 40 based on the same screening level (Schiotz weight tonometry) In these reports the incidence values ranged between 3 and 5 per cent (Table 1 – Reed & Bendor-Samuel 1957 Porter 1958 Bendor Samuel *et al* 1960)

In population examinations the incidence of high pressure values is as might be expected lower than among patients in an ophthalmic practice Stromberg (1962) for instance found 0 95 per cent with pressure values above 26 mm Hg (Schiotz) while Hollows & Graham (1966) saw 1 2 per cent with pressure values of 25 mm Hg or higher (applanation)

It is seen in Table 4 that pressures of 20 mm Hg or higher rose in frequency *with increasing age* For patients in the age classes of 35–44 and 45–54 the incidence was 4 5 and 4 1 per cent respectively while the age class of 55–64 showed a rise to 8 4 per cent and finally that of 65–74 a further rise to 16 8 per cent

For the pressure levels ≧ 22 mm Hg ≧ 25 mm Hg and ≧ 30 mm Hg the incidence was likewise seen to rise with increasing age though with the highest rise in the age class of 65–74

There was thus found a particularly pronounced rise in the incidence of high pressure *values about the age of 60 as also pointed out by Stromberg* (1962) and since recorded in various other series examined (Goedbloed 1961 Wright 1966 Hollows & Graham 1966 Bjornsson 1967 Nørskov 1970 a among others)

Pressures above the screening level were more frequently measured among females than among males 9 7 and 7 7 per cent respectively a difference which also prevailed within the individual age groups

A similar higher incidence among females has been found in two population series (*Stromberg 1962 and Hollows & Graham 1966*) *but has* also been recorded in relation to other examinations (Goedbloed 1961 Armaly 1965 and others)

However in the series under review pressure levels ≧ 22 mm Hg ≧ 25 mm Hg and ≧ 30 mm Hg were more frequent in principle among the males A similar higher incidence among males has been recorded for other series of patients from ophthalmic practices (Ascher 1962 Bjornsson 1967)

This deviation may possibly be related to the special recruiting of patients



Harald G A Gjessing

Harald Gustav Antonio Gjessing M D died on April 6th 19/0 without any previous illness

Gjessing was born in Drammen Norway on August 31st 1882 where he grew up and spent most of his life At the grammar school in Drammen he acquired the interest in classical languages which he always kept up After graduating in medicine in 1902 he served as general practitioner in many parts of Norway and also had several hospital appointments

After having spent some time in the eye department of Rikshospitalet, Oslo and in eye departments in Vienna he set up as practising ophthalmic surgeon in Drammen and remained there ever since His M D he obtained in 1920 by a paper entitled Clinical Studies on the Lens Gjessing went on innumerable study tours to most countries of Western Europe and to U S A He attended a large number of ophthalmological congresses and gave a good deal of lectures abroad During his travels he made many acquaintances and always took the opportunity to spread knowledge concerning Holth s iridencleisis

His intense interest in his own discipline is borne out by more than 60 publications mainly on glaucoma and a possible antagonism between cataract and senile macular degeneration In 19₃0 he published a major paper on Diagnostic and Differential Diagnostic Aspect in Diseases of the Eye

Gjessing became completely absorbed in whatever he undertook and this enthusiasm made him an excellent narrator to whom it was a pleasure to listen

He had been president of the Drammen Medical Association the Oslo Ophthalmological Society and the Norwegian Ophthalmological Society More over he was member of several foreign societies member of honour of the Ophthalmological Society of Copenhagen the Medical Society of Drammen and of the Norwegian Ophthalmological Society In 1962 he was awarded the Norwegian Order of Merit

Birger Malling

Table 5

Reasons for consulting ophthalmologist of 169 screening positive patients and 5 patients who later had the glaucoma diagnosis established

	Distribution of 169 screen ing positive patients	Distribution of 75 patients who had the glaucoma diagno sis established
Request for glasses	59	21
Conjunctival complaints	29	15
Conjunctival complaints during several years	18	9
Impaired vision	16	9
Headache	6	4
Rainbow rings or blurred vision	2	2
Presence of venous thrombosis	8	4
Request for pressure measurements in cases of familial occurrence of glaucoma	2	–
Cataract control	5	2
Referred by general practitioner as part of medic l examination	7	9
Sundry causes (e g entropion pterygium mouches volantes)	17	4

– all signs and symptoms of glaucoma at a fairly advanced stage – which relatively most often led to a diagnosis of glaucoma

The results of this investigation are thus in agreement with the current view that the information given by the individual patient on subjective troubles cannot be expected to contribute towards an early diagnosis of simple glau coma

Nevertheless we must realize that the patients in the series under review were selected in as far as they had all desired contact with an ophthalmo logist In this connection it is worth mentioning that on a glaucoma screening by applanation tonometry among members of the volunteer donor corps of Falster had the two donors with visual field defects recorded consulted the ophthalmologist spontaneously within the same period (Norskov 19 0 a)

Familial Predisposition

Occurrence of primary glaucoma among relatives is, according to Waarden

of these latter died within the observation period and nine failed to appear despite written requests being unwilling to any form of examination Finally in four cases examination was given up owing to a poor general condition or *high age In no more than one of these cases – a woman aged 86 –* were positive data available in support of the glaucoma diagnosis (glaucomatous optic disc)

Results

Grounds for Consulting an Ophthalmologist

It is a commonly held view that where the early diagnosis of simple glaucoma without field loss is concerned we cannot expect to be aided in singling out the glaucoma suspects on the basis of the reason given for consulting an ophthalmologist because patients may be inclined to delay consultation even after glaucomatous field loss

As however it is a question of great interest whether certain lines can be laid down from the data stated by the patients table 5 gives a survey of the 169 screening positive patients reasons for consulting an ophthalmologist

It is plain to see that such a survey yields no direct aid towards singling out the glaucoma suspects nearly two thirds having attended with the traditional complaints – conjunctival troubles or a request for new glasses

Among the patients under 45 years of age conjunctival troubles were the most frequent complaints while half of the patients in the age group of 40–64 *had problems with their glasses* With a single exception the patients complaining of impaired vision were over 65 There was no difference in principle between males and females

Table 5 also shows the distribution of the 75 patients who after the further examinations had the glaucoma diagnosis established (see p 853) It is seen that in this group too conjunctival complaints and a request for other glasses constituted a scant two thirds of the reasons for consulting an ophthalmologist

A similar preponderance of these two main causes of consultation among *patients with simple* glaucoma has been recorded by Touvinen (1961) Katavisto (1964) and Gassler (1965) A report made by Leydhecker (1968 a) for patients with gonioscopically open chamber angle showed that 60 per cent had no complaints while 40 per cent had symptoms In 23 per cent of the latter the majority within the group having the highest pressure level these symptoms corresponded to the prodromal ones in closed angle glaucoma

In the present investigation it was in fact rainbow rings around the light presence of central vein thrombosis of one eye headache and impaired vision

Routine tonometry among fairly young patients has also been recommended (Ascher 1962 Becker & Shaffer 1965)

It is difficult to say to which extent routine tonometry is carried through on the lines laid down Porter (1958) on inquiry among American ophthalmologists arrived at the result that 65 per cent of the 175 ophthalmologists asked employed routine tonometry Shapiro & Levine (1966) on the other hand and others noted a considerable slackness on this point among ophthalmologists

However only few ophthalmologists have at an early point of time expressed direct misgivings regarding the request for routine tonometry in ophthalmic practice (Schmidt 1959 Holm 1960 Ehlers 1960 Lauterstein 1960 1961 1962 1963 Walser 1965)

It is very important that the ophthalmologist who intends to adopt routine tonometry in his private practice is familiar to the greatest possible extent with the problems arising for both patient and doctor in relation to realisation of such a glaucoma prophylactic contribution

It is therefore surprising that as seen in table 1 fairly few papers are available in which an account is given of the experience gained from employment of routine tonometry among patients consulting an ophthalmologist.

In the present paper the results will be reported of a routine tonometry study using applanation tonometry carried out by an ophthalmologist in connection with glaucoma screening undertaken on the Island of Falster during the years 1960–1963

Present Investigations

The investigation comprised patients aged 35 or older from the Island of Falster who within the period from October 1 1960 to February 28 1962 consulted the only ophthalmologist of the island (E. Westerlund M D)

The only patients ruled out from the start were those with previously recognized primary or secondary glaucoma

Applanation tonometry concluded the eye examination otherwise concentrating on the cause of the patient s consulting the ophthalmologist. The measurements were performed between 12 30 and 5 p m

Just over half of the applanation measurements (61 per cent) were undertaken by the author and the remaining by one other examiner

The series comprised 2079 patients In table 2 we see the age and sex distribution related to that for the population of Falster (46 662 inhabitants on census September 26 1960) The patients within the age groups of 40–64

in arranging a recording of the 24 hour pressure variations to establish the glaucoma diagnosis Especially it is difficult to carry through the morning measurement Problems will also arise when the distance between ophthal mologist and patient is so great that admission to hospital for the purpose of regular recordings is contemplated

Of the patients in the series under review 55 had the 24 hour variations recorded during stay in the ophthalmic unit Three fourths of these were subjected to applanation tonometry by the same examiner while for practical reasons the remainder had measurements carried out by two skilled nurses using Schiotz weight tonometer (7.5 g)

The times of the maximum pressure values measured in the 55 patients have been set out in table 6 The last control value measured in the ophthalmic consultation was compared with those recorded within 24 hours of admission 11 a m – 4 p m 6 – 8 p m 7 a.m and 8 – 10 a m In the cases where the same maximum pressure value was measured at different times within the 24 hours the respective times were included It is seen in table 6 that the maximum value most often was measured in the ophthalmic consultation even compared to the total number of measured values plotted along the 24 hour curve The morning measurements were the second in frequency to give maximum pressure values whereas in rare cases only was a maximum pressure value recorded in the evening

A different way of assessing the relation between the out patient control pressure measurement and the 24 hour measurements during stay in hospital is that of determining the distribution of the values of 25 mm Hg or higher which according to the chosen criteria contribute largely towards establishing the diagnosis of glaucoma

Pressure values of 25 mm Hg or higher were measured in a total of 61 eyes (41 patients) In 39 of these (24 patients) such values were obtained both by

Table 6

Record ng of times for maximum pressure values in 55 patients (109 eyes) The 24 hour values measured dur ng the first 24 hours *stay in hospital* are compared with the last control values in ophthalmic practice

phthalm practice	during stay in hospital			
1 50 p m	11 a m – 4 p m	6 – 8 p m	7 a.m	8 – 10 a.m
t	15	1	23	15

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ROUTINE TONOMETRY IN OPHTHALMIC PRACTICE

I Primary Screening and Further Examinations for Diagnostic Purposes

BY

KNUD NØRSKOV

Within the past 15–20 years great efforts have been made to intensify the glaucoma prophylactic work by screening using tonometry carried through on different population groups (reviews by Leydhecker 1960 Ourgaud & Étienne 1961 Yusupov & Sumatokhina 1963 Posner & Fogland 1964 Segal & Skwierczynska 1967 and Pollack 1968)

A not previously recognized primary glaucoma is generally stated to have been disclosed in between 1 5 and 2 per cent of the examined persons aged over 40 In such examinations we operate with an arbitrary glaucoma concept which is based on the chosen glaucoma criteria but does not distinguish between presence of ocular hypertension and glaucoma with glaucomatous field loss

This is the background of the frequently advanced claim for routine tonometry of all patients aged 40 or older consulting ophthalmic medical practitioners no matter whether the eye examination raises suspicion of glaucoma (Phelps 1949 Hildreth & Becker 1957 Sloan 1957 Reed & Bendor Samuel 1957 Porter 1958 Sloan 1959 Leydhecker 1959 Bendor Samuel *et al* 1960 Schmidt 1960 Bruens 1961 Ascher 1962 Corydon Andersen 1964 Tronimopoulos *et al* 1965 Björnsson 1967 among others)

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burg *et al* (1961) to be expected in 17–18 per cent Westerlund (1947) in a Danish study found a percentage of 13

The patients included in the present investigation were not questioned about a familial predisposition in relation to the routine tonometry but such a questioning was carried through for the 169 patients with a screning pressure above 20 mm Hg A predisposition among near relations was found to exist in the families of eight patients (4 7 per cent) in five of whom a diagnosis of glaucoma was subsequently established

Pressure Control

In fixing an intra ocular pressure level for the individual patient we must bear in mind that as stated previously the estimation was based on a varying number of measurements distributed over control measurements in ophthalmic practice and measurements during out patient examination or stay in oph thalmic unit

In 56 patients (94 eyes) or 33 1 per cent of the 169 screening positive re peated pressure measurements gave 25 mm Hg or higher in support of the glaucoma diagnosis while in 23 patients (36 eyes) pressures of 30 mm Hg or higher were recorded on repeated measurements

For 111 patients (221 eyes) the results of control pressure measurements in ophthalmis practice were available This afforded a possibility of comparing screening pressure with control pressure measured at the same time of the day (between 1 and 5 p m) in order thus to get an impression of the consequences it would have for the patients concerned if on the basis of the same screening level of 20 mm Hg the control measurements had been chosen as the norma tive examination

In 13 or 11 7 per cent of the 111 patients the pressure values on the con trol examination were under the screening level in both eyes These cases would accordingly have been missed on a glaucoma screening based on the control pressure measurements

In two of these 13 patients a diagnosis of glaucoma (without field loss) was however subsequently established on the basis of the further examinations for diagnostic purposes This emphasizes the fact that by screening based on a single measurement we must not forget that glaucoma cases may be missed

It will furthermore be a commonly employed procedure in such cases as the 13 with a control tension below the screening level to characterize these values as false positive issues of the primary screening However the results of the present investigation showed the risk involved in refuting on the basis of a single control measurement a suspicion of glaucoma raised on routine tono metry

The ophthalmic medical practitioner will not infrequently have difficulty

Table 2

Age and sex distribution of patients who consulted ophthalmic medical practitioner *within the period from October 1 1960 to February 28 1967* seen in relation to the population of Falster

		25–39	40–64	≥ 65	Total
Population of Falster	males	3925	7394	2810	23715
census 26 9 1960	females	4218	7243	3154	23447
	Total	8143	14637	5964	46662
		25–39	40–64	≥ 65	Total
	males	51	484	211	746
Ophthalmic practice	females	102	838	343	1283
	Total	153	1322	554	2029

and within that over 65 represented 9 per cent of the total number of inhabitants within the age groups concerned At the census the age group of 40–64 and that over 65 included 51 and 47 per cent males respectively In the corresponding age groups of patients from the practice males constituted 37 and 38 per cent respectively The attendance was thus greater among females than among males as is often seen in an ophthalmic practice (Bjornsson 1967 Nørskov 1970 b)

Infectious eye diseases among others prevented tonometry in the cases of 97 patients (52 males and 45 females) In another 50 patients (19 males and 31 females) tonometry could not be carried through owing to nystagmus corneal changes or inadequate co operation

Thus 1882 of the 2029 attending patients or 92 8 per cent (males 90 5 per cent – females 94 1 per cent) were subjected to the routine tonometry aimed at The age and sex distribution is shown in table 3

None of the remaining 147 patients displayed signs of glaucoma

Screening Level

It had been decided that an applanation value of 20 mm Hg or higher in one or both eyes and a difference of 4 mm Hg or more between the two eyes motivated further examinations with a view to presence of glaucoma

Table 7

Distribution of 163 screening positive patients (335 eyes) according to appearance of optic disc and visual field

Visual field		OPHTHALMOSCOPY				
		normal	suspected glaucomatous	glaucomatous	not estimated	Total
1	normal	237	7	–	–	244
	baring of the blind spot	8	4	4	–	16
	arcuate scotoma without peripheral break through	–	1	4	–	5
3	arcuate scotoma with peripheral break through defects in nasal quadrants	–	1	2	–	3
4	loss of visual field in two or more quadrants	–	–	3	–	3
5	central rest temporal island or total blindness	55	3	2	4	64
6–7	visual field test not carried through					
		300	16	15	4	335

Table 1

Review of previous routine tonometries carried through in ophthalmic practices

	number	age	screening level calibration table Schiotz	suspects	%	GLAUCOMA DETECTED (PREVIOSLY UNKNOWN) with glauc field loss	%	without glauc field loss	%	Total	%	boderline cases	%
Phelps (1949)	720	> 45	< 3/5 5 27 mm Hg (1948)	–	–	18	2 5	19	2 6	37	5 1	–	–
Vaughan et al (1957)	5528	> 40	> 25 mm Hg (1948)	–	–	–	–	–	–	122	2 0	–	–
Hildreth & Becker (1957)	2000	> 40	–	49	2 5	–	–	38	1 9	38	1 9	–	–
Reed & Bendor Samuel (1957)	2000	> 40	≧ 25 mm Hg	99	5 0	28	1 4	30	1 5	58	2 9	7	0 4
Sloan (1957)	1184	≧ 40	≧ 26 mm (1954)	46	3 9	–	–	–	–	31	2 6	12	1 0
Corydon Andersen (1958)	800	> 50	≧ 22 mm Hg (1955)	18	2 3	–	–	–	–	8	1 0	10	1 3
I ortier (1958)	987	≧ 40	–	31	3 1	–	–	–	–	28	2 8	–	–
I orter (1958)	2000	> 40	≧ 25 mm Hg (1954)	61	3 1	22	1 1	22	1 1	44	2 2	–	–
Sloan (1959)	2100	≧ 40	≧ 26 mm Hg (1954)	77	3 7	–	–	–	–	45	2 1	30	1 4
Bendor Samuel et al (1960)	5000	> 40	≧ 25 mm Hg	249	5 0	32	0 6	43	0 9	75	1 5	–	–
Holmes (1961)	2000	≧ 40	–	–	–	–	–	–	–	23	1 2	–	–
Ascher (1962)	1000	≧ 21	≦ 4/5 5 (1955)	40	4 0	10	1 0	19	1 9	29	2 9	–	–
Gassler (1965)	3000	20–85	< 2 5/5 5 (1955)	98	3 3	–	–	–	–	98	3 3	–	–

24-hour measurements and in ophthalmic practice In the remaining 12 eyes (10 patients) values of 25 mm Hg or higher were recorded in the 24 hour pressure curve whereas the consultation values were below 25 mm Hg

In 10 eyes (7 patients) the reverse was the case the consultation values being here 25 mm Hg or higher and the 24-hour pressure level recorded be low 25 mm Hg

The stated results suggest that the ophthalmologist by basing his opinion on the out-patient control pressure values measured within the ordinary con sultation hours is in a better position to establish the glaucoma diagnosis than might be expected considering the fact that maximum values are stated relatively rarely to be recorded within the interval from 12 o clock to 6 p m the period during which the ophthalmic medical practitioner frequently sees his patients (Hager 1958 Drance 1960 Katavisto 1964)

This holds good when the pressure measurements are carried through under uniform external conditions The unexpected result in the present study is perhaps due to the measurements having not taken place under uniform external conditions the 24 hour measurements having been performed during stay in hospital where the tension might be expected to fall to a lower level than when the patient is in his usual environment (Hager 1958 Goldmann 1960 Ourgaud & Étienne 1961 Katavisto 1964)

In the cases of 87 patients it was however possible to compare a morning measurement (between 8 and 10 a m) during an out patient examination in the ophthalmic clinic with an afternoon measurement in the ophthalmic con sultation both carried out under uniform external conditions As might be expected the pressures measured at 25 mm Hg or higher rose in number from afternoon measurement to morning measurement namely from 8 to 16 eyes This result is in agreement with the current view that maximum pressures often are recorded at a point of time which is not within the usual consulta tion hours

Ophthalmoscopy

Table 7 shows the conditions of the optic discs estimated for 331 eyes (three patients were one eyed while in four cases ophthalmoscopy was impossible owing to cataractous changes)

The dics was normal in 300 eyes while in 15 it was glaucomatous and in 16 a glaucomatous disc was suspected

Ten patients or 5 9 per cent of the screening positive had a glaucomatous disc of one or both eyes while twenty had either a glaucomatous disc or one suspicious of glaucoma These constituted 11 8 per cent of the 169 patients subjected to further examinition or 1 1 per cent of the 1882 subjected to routine tonometry The percentage number is considerably smaller than in

pressure otherwise is within the normal range has been of no importance in the establishment of the glaucoma diagnosis

It rather seems that on demonstrating tension differences in patients with values otherwise within the normal range one should in the first place aim at precluding errors of measurement (Leydhecker 1958 *Jervey 1962*)

Patients with Applanation Values Above the Screening Level

169 patients or 9 0 per cent of the 1882 subjected to tonometry had applanation values measured of 20 mm Hg or higher The grouping was based on the eye for which the highest intra ocular pressure was recorded

The distribution according to age sex and pressure level is seen in table 4 In 89 patients (4 7 per cent) applanation values of 22 mm Hg or higher were

Table 4

Age and sex distribution of 169 patients with applanation value above the screening level

		35–44	45–54	55–64	65–74	75–84	≥ 85	Total	%
		377	55[illegible]	406	[illegible]09	188	[illegible]0	1882	
	males	5	4	7	1[illegible]	17	2	[illegible]	7 7
≥ [illegible]0	females	1[illegible]	[illegible]0	[illegible]7	3[illegible]	[illegible]2	1	11[illegible]	9 7
mm Hg	Total	[illegible]	24	34	[illegible]	39	3	169	–
	%	4 [illegible]	4 [illegible]	8 4	16 8	[illegible]0 7	–	9 0	–
	males	4	[illegible]	4	1[illegible]	14	2	38	[illegible]6
≥ [illegible]	females		10	9	18	13	1	[illegible]1	4 2
mm Hg	Total	4	12	13	30	27	3	89	–
	%	[illegible]	[illegible]	3[illegible]	9	14 3	–	4 7	–
	males	[illegible]	1	[illegible]		6	1	19	[illegible]8
≥ [illegible]5	females	–	[illegible]	4	1[illegible]	6	1	[illegible]8	2 3
mm Hg	Total	2	6	6	19	12	2	4[illegible]	–
	%	0 53	1 0	1 [illegible]	6 [illegible]	6 4	–	2 [illegible]	–
	males		1	1	[illegible]	[illegible]	–	9	1 3
≥ [illegible]	females		2	1	4	[illegible]	–	[illegible]	0 [illegible]
mm Hg	Total		3		9	4	–	18	–
			0.5	0 49	[illegible]9	2 1	–	0 96	–

Table 7

Distribution of [illegible] screening positive patients (335 eyes) according to appearance of optic disc and visual field

Visual field	OPHTHALMOSCOPY normal	suspected glaucomatous	glaucomatous	not estimated	Total
1 normal	237	7	–	–	244
baring of the blind spot	8	4	4	–	16
arcuate scotoma without peripheral break through	–	1	4	–	5
3 arcuate scotoma with peripheral break through defects in nasal quadrants	–	1	2	–	3
4 loss of visual field in two or more quadrants	–	–	3	–	3
5 central rest temporal island or total blindness	55	3	2	4	64
6–7 visual field test not carried through					
	300	16	15	4	335

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THE FREQUENCY OF POSITIVE DYE TEST IN BLIND CHILDREN

BY

MARIT LANGSET TORE MIDTVEDT and TOV OMLAND

Congenital and acquired systemic toxoplasmosis has been diagnosed with increasing frequency in recent years The classical signs of congenital toxoplasmosis i e hydrocephalus intracranial calcifications and chorioretinitis are well known Recent work however suggests that the most common form of congenital toxoplasmosis is that in which only the eyes are involved (*Fair* 1961) Ocular manifestations may also complicate acquired systemic toxoplasmosis (*Hogan* 1961 *Perkins* 1961 *Rieger* 1962 *Ramsell & Gamero* 1967)

Thus the eye seems to be one of the predilection places for Toxoplasma gondii If so this might be reflected in a higher frequency of positive dye test (DT) in blind individuals than in the normal population The present investigation shows the frequency of positive DT in a group of blind school children

Material and Methods

Sera were taken from all children at the Dalen State School for the Blind Trondheim Norway The children were from various districts of the country

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and were all within the age group 7 14 years Their visual acuity varied from complete blindness to 20/60

DT results from children in different departments at Rikshospitalet Oslo Norway and from school children living in the southern part of Norway were employed as a comparison group This material has been described in detail elsewhere (*Midtvedt* 1965)

The DT technique used was as described in previous papers (*Grondahl Midtvedt* & *Kolstad* 1962 *Midtvedt* 1965)

Results and Discussion

Table 1 presents the frequency of positive DT and the titre values in blind children In the age group 7-10 years 47 per cent show positive DT compared with 52 per cent in the age group 11 14 years In both age groups the titre values were low (1 4 or 1 10 in more than 80 per cent of the cases) particularly in the older group In the normal population the frequency of positive DT increases with age during childhood and the majority of the values is above 1 10 (*Midtvedt* 1965) The present findings might indicate that the blind children have been infected at an earlier age than those in the control group

Table 2 shows the frequency of positive DT in blind children as compared to the findings in a control group The data obtained permit a comparison by the X^2 test ($p < 0\ 001$) The test supports the assumption of a considerably higher frequency of positive DT in blind children than in the control group

It should be mentioned that only one of the blind children was previously diagnosed as a case of toxoplasmosis No further attempts were made to corre

Table 1
The frequency and titre values of positive DT in blind children

Age in years	No of	No of positive	Per cent of positive	Titre			
				1 4	1 10	1 40	1 200
7–10	30	14	47	6	4	3	1
11–14	29	15	52	10	5	0	0
Total	59	29	49	16	9	3	1

other series from ophthalmic practices where from one fourth to one third of those subjected to further examination presented disc changes (Porter 1958 Ascher 1962 Bjornsson 1967)

The two youngest patients with a glaucomatous disc were 57 and 59 years old respectively while the other patients were over 65

The youngest patient with a glaucoma suspicious disc was 41 years old

Visual Field Measurements

The measurements were carried through by campimetry using object sizes 2/2000 6/2000 and also 17/2000 if required In a few instances the campimetry was supplemented by measurement with Pflüger s perimeter

Of the 169 patients (335 eyes) only 141 har visual field measurements carried through of one or both eyes (271 eyes) Seven patients had died prior to control examination and nine were unwilling to continue examination while 12 (7 1 per cent) could not have a sufficiently accurate visual field measurement carried through Finally in the cases of nine eyes an estimation was forborne owing to presence of other disease – mainly cataract

The results of the visual field measurements are seen in table 7 The visual field was normal in 244 cases while visual field defects were observed in 27 eyes Pronounced visual field defects were present in no more than 11 of the latter

A total of 19 patients or 11 2 per cent of the screening positive had visual field defects of one or both eyes but extensive defects were seen in only eight of these 4 7 per cent)

The youngest patient with pronounced visual field defects was 48 years of age The remaining with grave visual field defects were aged over 65

Table 7 also shows the relation between the appearance of the optic disc and the result of the visual field measurement It is seen that all the eyes with a glaucomatous disc that were subjected to visual field measurement also presented a visual field defect Among these were five of the six cases with the gravest visual field defects

In half of the eyes whose disc was characterized as glaucoma suspicious the visual field was normal while the others had visual field defects mainly group 2

In eight eyes with discs characterized as within the normal range beginning visual field defects were disclosed (group 2) These consisted in all cases in baring of the blind spot with associated depression of the margins in the upper quadrants at object size 2/2000 Only two eyes also showed visual field defects at object size 6/2000

Gonioscopy

Gonioscopy was carried through on 147 patients who were grouped in con

This procedure was chosen not only to attain to an overall evaluation of the problems relating to employment of routine tonometry in ophthalmic practice but also because it was found difficult as carried through by Hildreth & Becker (1957) to definitely delimit a group of patients who after ocular examination without routine tonometry would be without suspicion of glau coma

In the endeavours to increase the effectiveness by employing routine tono metry and thereby reduce the number of missed glaucoma cases a tendency has manifested itself in the course of years towards using a lower screening level (Hunt 1966 Pollack 1968 Nørskov 1970 a)

In agreement with this a screening level of 20 mm Hg was chosen using applanation tonometry This involved however that every 11th patient (9 0 per cent) was suspected of glaucoma on this basis alone This is a considerably higher percentage than stated for any of the series from ophthalmic practice mentioned in table 1 In these the percentage numbers of screening positive ranged between 2 and 5 However as stated previously a direct comparison of these series is impossible

In this connection there may be reason to mention a calculation undertaken by Pollack (1968) on the basis of 18 screenings comprising 217 000 individuals He arrived at the result that with a screening level of 20 mm Hg routine tonometry gave 12 per cent screening positive Compared with this the in cidence in the series under review is by no means unrealistic especially not when one considers that the series consisted of patients from an ophthalmic practice

Proposals
Regarding Alterations of the Screening Procedure to Reduce the Number of Patients Referable to Further Examination

The very considerable number of screening positive patients when a screening level of 20 mm Hg is employed tempts one to choose a higher screening level

In this connection it is important to have the most exact knowledge pos sible of the relation between an alteration of the screening leved and the number of glaucoma cases consequently missed

In the series under review alterations of the screening level to 21 mm Hg 22 mm Hg and 25 mm Hg respectively would have reduced the number of patients referable to further examination to 73 53 and 28 per cent respectively of the original 169 with a screening pressure value of 20 mm Hg or higher At the same time the number of missed glaucoma cases when using the criteria stated p 853 would have constituted 9 16 and 47 per cent respectively of the original number of diagnosed glaucoma cases

Another solution might be that of graduating the screening level according

formity with the simplified classification employed by Gorin & Posner (1957) a wide open chamber angle is characterized by the entire trabecular network as well as the ciliary body being visible The chamber angle is characterized as *open when only the trabecular network is visible* but the ciliary body is *either not* visible at all or seen as a narrow band Finally the chamber angle *is described as narrow when neither the ciliary body nor the posterior two* thirds of the trabecular network *is visible The chamber angle is closed when* its structures behind Schwalbe s line are invisible

The grouping based on the appearance of the chamber angle and the patients ages is shown in table 8 It is seen that in 39 per cent (57 patients) the chamber angle was wide open in 44 per cent (65 patients) it was open and in 17 per cent (25 patients) narrow In no more than two patients did gonioscopy show a closed chamber angle

This distribution does not differ essentially from the statements for normals Thus Shaffer (1960) and Pietruschka (1959) found the percentage number of persons with a narrow chamber angle to be 12 and 15 respectively In drawing comparisons attention must however be given to differences regarding the basis of the classification in the series concerned

The number of individuals with a *narrow chamber* angle will rise with *increasing age (Leydhecker 1960 Duke Elder 1962)*

In the series *under review 11 per cent* (four patients) in the age group of *35-54 had a narrow chamber angle against 19* per cent *(21 patients)* in that *over 55*

Table 8

Gonioscopy Distribution according to appearance of *chamber angle* and patients ages

	35-54		≥ 55		Total	
	number	%	*number*	%	*number*	%
wide open angle	15	35	44	40	57	39
open angle	20	54	45	41	65	44
narrow angle	4	11	19	19	23	
closed angle	–	–	2		2	1

to age Thus 21 mm Hg has been suggested for the age class of 20–39 22 mm Hg for that of 40–59 and 24 mm Hg for that of 60–79 (Pollack 1968)

If in the present investigation we chose on the same lines to alter the screening level to 22 mm Hg for patients between the ages of 35 and 64 and to 25 mm Hg for patients over 65 the number of patients within the two age groups referable to further examination would fall to 39 per cent (35–64 years) and 35 per cent (over 65) of the original 169 patients with a screening pressure of 20 mm Hg or higher At the same time the number of false negative cases would constitute 24 per cent (35–64 years) and 44 per cent (over 65) of the original number of diagnosed glaucoma cases

If we adopt the procedure of graduating the screening value we must also consider an adjustment according to the patient s sex and the time of the screening tension measurement

The results of the present investigation thus give plain evidence of our dilemma as employment of a higher screning level possibly graduated according to age sex and time of the day does give a welcome reduction of the number of patients referable to further examination but at the expense of missed glaucoma cases judged by the glaucoma criteria chosen

A procedure frequently employed for lessening the efforts required after routine tonometry is that of letting the result of a single control measurement decide whether more time consuming further examinations are to take place

If this procedure had been employed in the present study it would have been possible to rule out 12 per cent of the 111 patients who had the tension controlled within the same period of the day However the further examinations revealed that such a procedure would result in missed glaucoma cases which in fact had been disclosed at the initial routine tonometry

How Can the Ophthalmologist Disclose Glaucoma Cases With No Glaucomatous Field Loss Without Employing Routine Tonometry?

In relation to the present study the results of which plainly show the enormous work with which the ophthalmologist adopting routine tonometry is charged it seems reasonable to deal with the other chances the ophthalmologist has of tracing glaucoma before glaucomatous field loss has set in

The patient s history in its widest sense the central visual acuity ophthalmoscopy and visual field measurement are at the ophthalmologist s disposal for this purpose

In cases of closed angle glaucoma valuable anamnestic data are often available but to judge from the present investigation we cannot expect much aid from the information given by patients with simple glaucoma concerning the cause of their application at any rate not till the patient suffers from glaucoma with field loss

Provocative Tests

A Water provocative test 135 patients (269 eyes) or 80 per cent of the 169 screening positive were subjected to water provocative test Of the 34 patients who did not have this test carried through six had the diagnosis established otherwise while five objected to the test and in three cases the test was forborne owing to the patients poor general condition In the remaining cases no further examination was undertaken in the ophthalmic unit Seven patients were unable to drink a whole litre of water A rise of 8 mm Hg or higher was obtained in 55 eyes corresponding to 20 4 per cent of the water provocative tests carried out Of the subjects reacting positively to the test 75 per cent were over 65 years of age

A detailed account of the experience gained from the water provocative test in the present series of screening studies has been given in a previous report (Nørskov 1967 a)

B Priscol provocative test This provocative test was only offered to patients admitted to the ophthalmic unit It was carried through for 36 (68 eyes) of the 62 hospitalized patients

Rises of 11 mm Hg or higher were released in 28 eyes or 41 2 per cent Details concerning the results of the present investigation have been given in a previous publication (Nørskov 1966)

C Pupil dilatation tests The mydriasis tests held no central position in the present work which concentrated on tracing simple glaucoma by routine tonometry Such tests were preferably carried through on patients staying in hospital thus on a total of 40 patients in relation to pupil dilatation for retinal photography (cyclogyl (cyclopentolate) or homatropine 1 %)

Finally a dark room test was available for two patients – in both with a negative result

In ten patients whose chamber angle was characterized as narrow the test gave no pathological alteration A rise of 8 mm Hg or higher was released in three (six eyes) of the 30 patients with open or wide open chamber angle The maximum rise was 17 mm Hg

These reactions to pupil dilatation despite a gonioscopically open chamber angle must be regarded as unusual though such have been recorded by various writers (Leydhecker 1955 Galin 1961 Harris 1968)

Simple Glaucoma

Presence of one or more of the following criteria were required for establishment of the glaucoma diagnosis

1 Distinct marginal cupping of the optic disc
2 Reproducible glaucomatous visual field defects

If further on the basis of our knowledge concerning the relationship be tween glaucoma and central vein thrombosis glaucoma and diabetes, glaucoma and high myopia glaucoma and thyroid dysfunction as well as glaucoma and pseudo exfoliation as suggested by Becker & Shaffer (1965) we aim at utiliz ing the histories to suspect glaucoma in such cases then 25 patients or 15 per cent of the 169 caught by routine tonometry would have been suspects Of these 16 patients or 21 per cent of the 75 newly diagnosed glaucoma cases subsequently had the glaucoma diagnosis established

Another eight patients gave information on a familial predisposition to glaucoma The diagnosis was established in five or 6 7 per cent of the 75 diagnosed glaucoma cases In Leydhecker s (1959) and Bertelsen s (1965) series glaucoma occurred among near relations in 8 2 and 13 per cent respectively of the patients with diagnosed glaucoma

There seems in other words to be a certain possibility of rendering the work with glaucoma tracing more efficient by utilizing the anamnestic data on the stated lines

Impaired central visual acuity caused by glaucoma occurs only at an ad vanced stage of the disease but this may in certain cases give occasion to disclosure of glaucoma without field loss of the other eye

Ophthalmoscopy is the earliest examination employed for glaucoma screen ing Though ophthalmoscopy is rather unsuitable for disclosing glaucoma with out field loss many ophthalmologists still regard it as the most important weapon within the field of glaucoma prophylaxis among others (Holm 1960 Colenbrander 1960 Graham & Hollows 1966 Walker 1966 Blaxter 1966)

Use of ophthalmoscopy is however rendered difficult by the gradual transi tion from physiological to pathological cupping

It is generally stated that if the cupping covers more than 60–70 per cent of the disc area glaucoma must be suspected (Leydhecker 1960 Snydacker 1964 Becker & Shaffer 1965) In agreement with this a screening based on ophthalmoscopy alone will according to Snydacker (1964) raise suspicion of glaucoma in 4 per cent of persons aged over 40

However in the present series the incidence was no more than 1 1 per cent and in those of Porter (1958) Ascher (1962) and Bjornsson (1967) 1 0 1 1 and 1 7 per cent respectively This seems to indicate that the ophthalmologist who employs both ophthalmoscopy and routine tonometry for screening in variably takes account of the routine tonometry value when evaluating the optic disc This also explains why in the present study only one glaucoma suspicious disc was found among the subjects with tension values below the screening level The found percentage of glaucoma suspicious discs thus is no indication of the number of discs giving rise to suspicion of glaucoma when ophthalmoscopy alone is employed for screening

As a visual field measurement usually is not included in an ordinary eye

3 Intra ocular pressures ≧ 25 mm Hg
4 Rises ≧ 8 mm Hg in response to water provocative test
5 Rises ≧ 11 mm Hg in response to priscol provocative test
6 Rises ≧ 8 mm Hg in response to mydriasis test
7 Rises ≧ 10 mm Hg in response to dark room test

In the cases of 75 patients representing a scant half of the 169 patients traced by routine tonometry a diagnosis of glaucoma was in agreement with this rendered likely in 133 eyes as shown in table 9 where the distribution according to criteria is indicated

In half of the cases only one criterion of glaucoma was present while in

Table 9

Criteria for establishing the glaucoma diagnosis in 133 eyes (75 patients)

1 Criterion present	
pressure values ≧ 25 mm Hg	37
water provocative test ≧ 8 mm Hg	18
priscol provocative test ≧ 11 mm Hg	10
visual field defect	1
mydriasis test ≧ 8 mm Hg	1
2 Criteria present	
pressure values ≧ 25 mm Hg + visual field defect	6
pressure values ≧ 25 mm Hg + pos water provocative test	24
pressure values ≧ 25 mm Hg + pos priscol provocative test	8
pressure values ≧ 25 mm Hg + pos mydriasis test	1
visual field defect + glaucomatous optic disc	4
pos water prov test + pos priscol prov test	1
pos water prov test + visual field defect	2
pos priscol prov test + visual field defect	2
3 Criteria present	
pressure values + glaucomatous disc + visual field defect	6
pressure values + visual field defect + pos priscol prov test	1
pressure values + visual field defect + pos water prov test	2
pressure values + pos mydriasis test + pos priscol prov test	1
pressure values + pos water prov test + pos priscol prov test	2
pressure values + pos mydriasis test + pos water prov test	1
4 Criteria present	
pressure value + glau disc + pos mydriasis test + pos water prov test	2
Criteria present	
pressure values + glaucomatous optic disc + visual field defect + pos water prov test + pos priscol prov test	3

examination in ophthalmic practice a knowledge of the relation between the appearance of the optic disc and the extent of the visual field defect will be a factor of great importance from a glaucoma prophylactic aspect. Traditionally a fair correlation is claimed to exist between the two variables (Traquair 1938 Harrington 1964) though exceptions have frequently been stated (Aulhorn & Harms 1960 Armaly 1962 Shutt *et al* 1967 among others)

In agreement with this the series under review showed as a main rule a fair correlation between the appearance of the optic disc and the extent of the visual field defect (table 7) but in six patients (eight eyes) baring of the blind spot was found despite normal discs

In making up one s mind about the usefulness of visual field measurement as a primary screening test one must not forget that it is particularly elderly glaucoma suspects who are subjected to this test – in the present series more than half were over 65 Visual field measurement had to be completely abandoned in 7 per cent but this figure by no means reflects the difficulties not infrequently prevailing with regard to making out whether a patient of this age group has a minor visual field defect

Finally in this connection it must be a matter of great interest for the ophthalmologist to realize how many glaucoma cases will be missed by employing a procedure which does not include routine tonometry

According to Hildreth & Becker the missed glaucoma cases constitute 1 9 per cent in the age group over 40 Other ophthalmologists have arrived at between 1 and 3 per cent missed glaucoma cases dependent on the chosen glaucoma criteria in series from ophthalmic practices

No such grouping has been undertaken of the series under review Nevertheless we had a possibility of forming an impression of the number of diagnosed cases before the introduction of routine tonometry compared with that after the introduction

During a five year period prior to the introduction of routine tonometry on Falster on an average 7 8 fresh glaucoma cases were recorded annually while the number of patients with glaucomatous field loss diagnosed annually within the routine tonometry period amounted to 8 4 annually

This means that without use of routine tonometry few or no glaucoma cases with no field loss will be disclosed while at the same time all with field loss seem to be detected

Reflections in Relation to Further Examinations

The condition that routine tonometry can have the desired glaucoma prophylactic value is that all the patients suspected of glaucoma by this procedure do have further examinations carried through

The request for control examination should therefore be so urgent that the

only 18 eyes (14 per cent) not less than three criteria were available to justify establishment of the diagnosis In this connection we must however make allowance for the greatly varying frequency of accomplishment for the different methods of investigation

The crieterion most frequently present was that of pressure values recorded at 25 mm Hg or higher which occurred in 94 eyes

In 58 patients such high values were a bilateral phenomenon while 17 patients had the glaucoma diagnosis established for one eye only In 12 of these cases the other eye was characterized as a borderline case and in four as normal One patient was one eyed

A comparison of the incidence of closed angle glaucoma with that of simple glaucoma showed as might be expected a considerable predominance of the latter form only two patients having displayed a gonioscopically closed angle

Table 10 shows the age and sex distribution of the 75 patients The total number of diagnosed glaucoma cases constituted 4 0 per cent of the original number of examined patients The incidence was found to rise with increasing age No cases occurred in the age group under 40 but the incidence rose from 1 4 per cent in the age group of 45–54 to 3 2 per cent in that of 55–64 The highest rise from 3 2 to 9 0 per cent was noticed from the age group of 55–64 to that of 65–74

For males and females the diagnosed glaucoma cases constituted 4 2 and 3 9 per cent respectively The highest rise in number for both males and females was seen from the age group of 55–64 to that of 65–74 Otherwise the distribution varied somewhat within the individual age groups

Table 10

Age and sex distribution of 75 patients who had the glaucoma diagnosis established

	males		females		Total	
	number	%	number	%	number	%
35–44	2	1 6	2	0 80	4	1 1
45–54	2	0 92	6	1 6	8	1 4
55–64	4	3 0	9	3 3	13	3 2
65–74	11	11 3	17	8 0	28	9 0
75–84	8	8 8	12	12 4	20	10 6
≥ 85	1	(11 1)	1	(9 1)	2	(10 0)
Total	28	4 2	47	3 9	75	4 0

patients concerned really do attend At the same time however one must take care not to render the patient apprehensive

In the present study we proceeded by explaining to the patient that the tension in the eye was a little above normal and that on this account we advised control within 1–3 months However by this procedure 30 per cent failed to appear Other ophthalmologists have had difficulties of the same kind in their practices Reed & Bendor Samuel (1957) and Bendor Samuel *et al* (1960) stated that 30 and 38 per cent respectively of their patients failed to attend

The experience gained from the present investigation goes to show that the number of absentees can be reduced by proposing control after one month at most and preferably at a fixed date Summoning by letter effected that 82 per cent of the absentees were examined later

In planning the further examinations we must aim at a reasonable balance *between the examinations judged to be necessary for taking a decision on the* suspicion of glaucoma raised by routine tonometry and the examinations that are practicable in consideration of work load economy and the patient s psyche

In *arranging* the further examinations we *originally* aimed at a procedure fitting in with the conditions available to the ophthalmologist with no support from an ophthalmic unit The reasons why hospitalisation was nevertheless employed were partly a desire for rapid accomplishment of the examination in question and partly to render the examination more convenient to the patients living far away from the ophthalmologist

Many of the patients were however unwilling to accept admission to hospital As many as one fourth of the patients whose examination had been arranged refused admission

On the other hand it was often difficult to make the patients who had been through the entire series of examinations accept that the results achieved afforded no basis for any treatment of their eyes

If however the ophthalmic medical practitioner is to carry through further examinations on the lines stated in the present paper which by no means *can* be characterized as ideal this cannot be done without a radical change of the usual working rhythm The consultation hours will have to be prolonged in consequence of the many control pressure measurements and provocative tests and *24-hour pressure measurements cannot take place* within the usual consultation hours

The provocative tests play a prominent role in the diagnosis of glaucoma without field loss However their use has the definite disadvantage that from a clinical aspect the tests afford no possibility of foretelling which patients are liable to future development of visual field defects

Regarding tonography different views prevail on the basis of follow up

As shown in table 11 12 patients (eight males and four females) had glaucoma at a fairly advanced stage that is with a glaucomatous optic disc or more extensive visual field defects These constituted 0 64 per cent of the 1882 subjected to routine tonometry the incidence being 1 2 per cent for males against only 0 33 per cent for females By way of comparison it may be mentioned, as seen in table 1 that the incidences stated of glaucoma with glaucomatous field loss in the series from ophthalmic practices ranged from 0 6 to 2 5 per cent

The three youngest patients were 48 57 and 59 years of age respectively while the remaining were over 65

12 newly diagnosed cases of glaucoma at an advanced stage within the period from October 1 1960 to February 28 1962 corresponds to 8 4 patients annually

By way of comparison it may be stated that prior to the introduction of routine tonometry 7 8 fresh glaucoma cases were recorded annually over a five year period on the Island of Falster

Regarding the relation between screening tension and diagnosing of glaucoma it appeared that in three cases despite screening tensions below 20 mm Hg (in one eye) a diagnosis of glaucoma was subsequently established of this eye. In one case the eye even presented both cupping of the disc and fairly extensive visual field defects

Choice of 21 mm Hg as the screening level would have reduced the number of patients for further examination from 169 to 123 In other words only 73 per cent of the original number of patients would have been registered for further examination The number of patients with diagnosed glaucoma would

Table 11

Age and sex distribution of 12 patients who had a glaucomatous optic disc or fairly extensive visual field defects

	35–44	45–54	55–64	65–74	75–84	Total
males	–	–	2	4	2	8
females	–	1	–	2	1	4
Total	–	1	2	6	3	12

examinations Linner & Stromberg (1964) and Armaly (1969) hold that no definite conclusions can be drawn from the results of tonography whereas Leydhecker (1968 b) claims to have demonstrated a relationship in this respect

The problems relating to employment of the priscol test and the water provocative test have been discussed in two previous papers (Nørskov 1966 1967 a) These studies showed that of the two tests when employed on the same patients and with limits of a positive issue fixed at 11 mm Hg and 8 mm Hg respectively the priscol test would most frequently cause a pathological rise (41 and 22 per cent respectively) in agreement with Leydhecker's statements (1955) The patients included in the present investigation proved however to dislike the priscol test so much that the author on this account found the test to be unsuitable for ordinary clinical use

A tendency prevails towards increasing the demands on the provocative tests Thus for instance attention has been given to the question whether a graduation according to age of the limit of a pathological rise is required (Wesberry *et al* 1966 Ballin & Becker 1967) In the series under review 75 per cent of the positive results of the water provocative tests occurred in persons aged over 65

Classification of Patients with Ocular Hypertension in Glaucoma Borderline Cases and Normals

Such a classification is rendered difficult by the disagreement regarding the definition of glaucoma without field loss

Further various screenings are somewhat difficult to evaluate because the information available concerning the glaucoma criteria is not sufficiently accurate to allow of an estimate of the basis on which the stated incidence of glaucoma has been attained to

The glaucoma criteria chosen in the present investigation are in fair agreement with those stated in other Scandinavian papers dealing with routine tonometry studies (Corydon Andersen 1958 Bertelsen *et al* 1965 Nørskov 1967 b 1970 a Bjornsson 1967 Jensen 1968)

In the series under review the incidence of glaucoma was 4 0 per cent among patients aged over 35 In the other series from ophthalmic practices the incidences stated ranged from 1 to 5 per cent (table 1)

The incidence for males was 4 2 per cent and that for females 3 9 per cent These figures are in fair agreement with those given by Ascher (1962) – males 3 3 per cent and females 2 6 per cent and Bjornsson (1967) – males 5 0 per cent and females 4 7 per cent and with the usual statements of the distribution of simple glaucoma between males and females (Leydhecker 1960)

The incidence rises with increasing age even considerably so after the age

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glaucoma per October 1 1960 prior to the introduction of routine tonometry was 0 30 per cent (61 patients) for persons aged over 40 The prevalence of *simple glaucoma was 0 23 per cent (48 patients)*

It is shown in table 12 that Kurland & Taub (1957) and *Corydon Andersen (1958), in similar reports from geographically well defined territories found* a prevalence of primary glaucoma in the same age group of 0 34 per cent and 0 45 per cent respectively

For the sake of comparison the table also gives the prevalence of primary glaucoma with associated visual field defects disclosed on two population *examinations* Stromberg (1962) *examined 80 per cent of the inhabitants aged*

Table 12

Prevalence of primary glaucoma in geographically well defined population groups

A	population group	number of inhabitants	PREVALENCE	
			primary glaucoma	*simple glaucoma*
Kurland & Taub (1957)	Rochester *Minnesota USA*	9521 (≥ 45 yrs) (31 12 1954)	0.34 %	0 27 %
Corydon Andersen (1958)	Horsens *Denmark*	11 634 (≥ 45 yrs) (31 12 1957)	0 45 %	–
Nørskov (1960)	Falster Denmark	20 601 (≥ 40 yrs) (1 10 1960)	0 30 %	0 23 %
B				
Stromberg (1962)	*Skovde* Sweden	9288 (≥ 40 yrs)	0 38 %	–
Hollows & Graham (1966)	Rhondda Valley Wales	4608 (40–75 yrs)	0 51 %	0 43 %

A calculated from occurrence of clinically recognized glaucoma in the territory concerned

B *population studies*

at the same time have been reduced from 75 to 68 This means that 9 per cent of the original number of glaucoma cases would have failed to be recognized among which three with glaucomatous field loss

With a screening level of 22 mm Hg only 89 patients or 53 per cent of the original number would have been subjected to further examination At the same time however the glaucoma diagnosis would not have been made in 12 cases or 16 per cent of the original number of glaucoma cases Four of these patients had glaucoma with field loss

Finally by altering the screening level to 25 mm Hg the number of patients for further examination would be reduced from 169 to 47 This means that only 28 per cent of the original number would have been further examined At the same time the number of diagnosed glaucoma cases would have been reduced from 75 to 40 In other words the missed glaucoma cases would have constituted 47 per cent of the original number diagnosed Seven of these patients had glaucoma with field loss

Another possibility is that of graduating the screening value according to the patient s age If thus the screening level for patients between the ages of 35 and 64 had been altered to 22 mm Hg the number of patients to be subjected to further examination would have been reduced from 75 to 29 Accordingly no more than 39 per cent of the original number from this age group would be referable to further examination At the same time the number of patients with diagnosed glaucoma would have been reduced from 25 to 19 In other words 24 per cent of the original number of newly diagnosed glaucoma cases would have been missed including two with glaucomatous field loss

If 25 mm Hg had been chosen as the screening level for the age group over 65 the number of patients for further examination would have been reduced from 94 to 33 or no more than 35 per cent of the original number would have been referred to further examination At the same time the number of diagnosed glaucoma cases would have been reduced from 50 to 28 Thus 44 per cent of the original number of newly diagnosed glaucoma cases would have been missed including three with glaucomatous field loss

In tracing glaucoma one should further according to Becker & Shaffer (1965) utilize the anamnestic data available knowing that a relationship exists between glaucoma and central vein thrombosis glaucoma and diabetes glaucoma and high myopia glaucoma and thyroid dysfunction as well as glaucoma and pseudo exfoliation

Among the patients with screening values above 20 mm Hg twelve had diabetes eight central vein thrombosis three high myopia one thyroid dysfunction and one pseudo exfoliation A diagnosis of glaucoma was established in six of the patients with diabetes seven with central vein thrombosis two with high myopia and one with pseudo exfoliation

of 60 Among the patients ranging in age from 65 to 74 glaucoma was in fact diagnosed in every 11th of the patients seen Ascher (1962) found the incidence to be 6 7 per cent among patients aged over 60 Björnsson states 6 6 and 10 per cent for the age groups of 60–69 and 70–79 respectively

The borderline cases constitute an ill defined group of patients within the pressure range of 20–24 mm Hg The work with which the ophthalmologist going in for routine tonometry is burdened depends greatly on the size of this group which also detemines the number of patients to be troubled with continual control

Disagreement prevails regarding the chance that glaucoma with field loss may develop from this group of borderline cases Various ophthalmologists who have undertaken screenings take the chance to be so great that they have included the borderline cases in their calculations of the glaucoma incidence among others (Brav & Kirber 1951 Corydon Andersen 1958 Packer *et al* 1959 Dunbar & Goldberg 1960) Linner & Stromberg (1964 1967) on the other hand state that persons with a moderate ocular hypertension rarely develop glaucoma with field loss

Adoption of the view that borderline cases have such a great chance of developing into glaucoma with field loss would with the criteria chosen in the present study have involved continued control of a number of patients of the same order as those with manifest glaucoma i e 4 1 per cent of the 1882 patients subjected to routine tonometry The incidence is however lower – 0 4 to 1 4 per cent – in the series from ophthalmic practices in which this has been calculated for the borderline cases (table I)

The number of borderline cases depends in some measure on the extent of further examinations the criteria for establishing the glaucoma diagnosis and also on the criteria chosen for normality In the present study it was required that all the control examinations gave values within the normal range including tension measurements below 20 mm Hg

If thus in the present investigation a value of 21 mm Hg had been regarded as within the normal range the incidence of borderline cases would have fallen from 4 1 to 2 6 per cent

Thus in attempting to form an estimate of the usefulness of routine tonometry it is highly inconvenient that such great uncertainty also prevails regarding the differentiation between borderline cases and normals

Relation between Glaucoma with and without Glaucomatous Field Loss

Our knowledge concerning the prevalence of glaucoma with field loss is very deficient despite comprehensive statistics from ophthalmic clinics (Leydhecker 1960) and results reported of a considerable number of screenings

On the Island of Falster the prevalence of clinically recognized primary

Normals

This group comprised patients for whom the total number of control examinations of both eyes gave results within the normal range including control pressure measurements below 20 mm Hg

16 patients (15 males and 1 female) were included in this group This means that 9 5 per cent of the 169 screening positive patients subsequently could be declared normal The result of the screening test must thus in these cases be characterized as false positive

Borderline Cases

This group comprised the cases in which the examinations carried out and the criteria laid down for establishing the glaucoma diagnosis or characterizing the condition as normal (see above) afforded no basis for confirming or refuting a diagnosis of glaucoma

A total of 78 patients (141 eyes) were included in this group constituting 4 1 per cent of the original number examined 23 males (3 4 per cent) and 55 females (4 6 per cent)

In 63 cases this phenomenon was bilateral while in 13 one eye was normal Two patients of this group were one eyed.

As stated previously 12 patients with one eye characterized as a borderline case and the other as glaucomatous were included in the glaucoma group

The demand for control tension values below 20 mm Hg as a criterion of normality contributed particularly to the considerable number of borderline cases By altering this demand to below 21 mm Hg the number of borderline cases would have been greatly reduced from 78 to 49 or from 4 1 to 2 6 per cent of the original number of examined patients

Discussion

A direct comparison of the series mentioned in table 1 originating from other ophthalmic practices and that constituting the basis of the present investigation has been rendered difficult by differences regarding a number of the factors influencing the results achieved These factors are such as differences in composition of the groups of patients examined from the individual practices the screening level chosen the extent of further examinations and the glaucoma criteria employed

In the study under review the practice series was preserved as an entity similarly as were most of the series included in table 1 The only patients ruled out were those with previously recognized glaucoma and patients with eyes in a state of acute ocular inflammation

After further examinations including provocative tests the glaucoma diagnosis was established in 4.0 per cent (75 patients). No more than 12 of these patients (0.64 per cent) had glaucoma with a fairly extensive field loss. Only two patients had closed angle glaucoma.

The borderline cases constituted 4.1 per cent (78 patients). 16 patients (9.5 per cent of those subjected to further examinations) were characterized as normal, all the control examinations having revealed normal conditions including tension values below 20 mm Hg.

Under the impression of the enormous work with which the ophthalmologist going in for routine tonometry is burdened, suggestions are advanced for *modifications of the screening procedure. In addition mention is made of* other possibilities of disclosing glaucoma without field loss.

Furthermore the *difficulties are stated of distributing patients with ocular hypertension in the groups of glaucoma cases, borderline cases and normals. These difficulties seem to give a reasonable explanation of the considerable difference between the prevalence of clinically recognized glaucoma on the* Island of Falster *(0.30 per cent for persons aged over 40)* and the great number of newly diagnosed glaucoma cases found during the present investigation by examining a group of patients constituting 9 per cent of the population of Falster aged over 40.

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Table 9

A comparison of the frequency of positive DT in blind children at Dalen State School for the Blind and in a control group

Age in years	Group	No of sera	No of positive	Per cent of positive	Probability[a]
7-10	Dalen	30	14	47	P < 0 001
	Control	83	11	13	
11-14	Dalen	29	15	.2	P < 0 001
	Control	117	20	17	

) χ^2 test

late DT titres and diagnosis There are obvious difficulties in diagnosing ocular toxoplasmosis in blind children showing a positive DT The prevalence of past or persistent toxoplasmosis in the general population reduces the diagnostic va lue of DT in older children The problems of causal relationsships might be elucidated by further investigations especially in younger age groups

Summary

The frequency of positive DT in blind children at the Dalen State School for the Blind Norway has been studied This frequency was significantly higher than in a control group

Acknowledgement

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over 40 in Skovde Sweden while Hollows & Graham (1966) examined 91 9 per cent of the persons aged between 40 and 75 living in Rhondda Valley Wales

As seen in table 12 there is fair agreement between the prevalence of clinically recognized primary glaucoma and the prevalence of primary glaucoma with visual field defects recorded in relation to the population examinations

It is therefore surprising that on Falster routine tonometry in an ophthalmic practice of a group of patients constituting 9 per cent of the population aged over 40 revealed in the course of 18 months 75 fresh cases of glaucoma on the basis of the chosen criteria which are those commonly employed at routine tonometry in the Scandinavian countries

The most reasonable explanation of this problem is that with the diagnostic aids available at present we have only a slight possibility of distinguishing between ocular hypertension and glaucoma which later will develop visual field defects

The final answer to the question of the value of routine tonometry can however only be given on the basis of follow up examinations carried through in relation to glaucoma screening In a future paper an account will be given of a recently concluded five year follow up carried out in continuation of the present investigation

Summary

The present study is based on routine tonometry carried out on 1882 patients aged over 35 who consulted the only ophthalmologist on the Island of Falster (93 per cent of the number attending)

Patients with previously recognized glaucoma and patients with acute ocular inflammatory states were ruled out

169 patients (9 0 per cent) had an applanation value recorded of 20 mm Hg or higher

Presence of one or more of the following criteria was required to establish the diagnosis

1 Distinct marginal cupping of the optic disc
2 Reproducible glaucomatous visual field defects
3 Pressure values measured $\geqq$ 25 mm Hg
4 Water provocative test $\geqq$ 8 mm Hg
5 Priscol provocative test $\geqq$ 11 mm Hg
6 Mydriasis test $\geqq$ 8 mm Hg
7 Dark room test $\geqq$ 10 mm Hg

Table 3

Comparison of the pressure level on primary outpatient control examination with that on follow up examination after five years (136 eyes of 68 untreated patients)

	follow up examination			
	< 20 mm Hg	20–21 mm Hg	22–24 mm Hg	≧ 25 mm Hg
primary out patient control examination				
<–20 mm Hg	37	21	7	1
20–21 mm Hg	5	22	16	4
22–24 mm Hg	2	5	4	5
≧ 25 mm Hg	1	1	1	4

author in a previous study (1970a) This indicates that the intra ocular pressure cannot be taken as a fixed value but will undergo variations

Ophthalmoscopy 220 eyes (110 patients) were to be subjected to ophthalmo scopy which however could not be carried through for six eyes

Ten eyes were found to have a glaucomatous optic disc in agreement with the ophthalmoscopic finding on the primary screening

Out of seven eyes whose discs had originally been characterized as glaucoma suspicious four had developed a glaucomatous disc while the conditions re mained unchanged in the remaining three eyes

Of the 197 eyes with discs originally characterized as normal 192 had re mained unchanged while in three a glaucomatous disc had developed and in two a disc suspicous of glaucoma

Visual field measurements 101 patients had the visual fields measured at the follow up An estimation was impossible in the cases of nine patients owing to failing co operation or to presence of cataract or senile macular degeneration

The primary screening revealed visual field defects in 15 patients (22 eyes) In 11 patients (16 eyes) the defects were at the initial stage while in four (six eyes) they were at a more advanced stage

In six of the patients with beginning visual field defects (eight eyes) who had had baring of the blind spot recorded at the primary screening despite normal discs the visual field defects were no longer visible on the follow up examina tion This is the more surprising because a pressure level below 20 mm Hg had been obtained neither with nor without treatment This observation stresses the doubtful value of considering baring of the blind spot as an early sign of glau

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In five patients (eight eyes) the primary screening had revealed not only beginning visual field defects but also a glaucomatous or glaucoma *suspicious* optic disc These patients were all under treatment In four eyes the follow up examination showed progression *of the visual field defects* while in the four others the conditions had remained unaltered

Of the six eyes (four patients) with primarily recorded fairly advanced visual field defects three (two patients) showed progression of the visual field defects despite treatment and a pressure level of 20–21 *mm Hg* while in the other three eyes (two patients) the conditions had *remained unaltered*

Out of 86 patients followed up who originally had normal discs and visual fields two (two eyes) developed visual field defects *during the observation* period

An over all assessment of the course during the observation period based on ophthalmoscopy and visual field measurement gave progression of the glaucoma in ten (14 eyes) of the 110 patients followed up Seven patients ranged in age from 59 to 72 at the time of the screening The youngest patient was 57 and the oldest 81

Regulation of the tension to below 20 mm Hg within *the observation period* was obtained in two eyes only while in nine eyes a level between 20 and 24 mm Hg was recorded and finally in three eyes 25 mm Hg or higher

In four (seven eyes) of the ten patients showing progression there was progression of existing visual field defects or development of optic disc changes observed by ophthalmoscopy Two patients (three eyes) had both glaucoma and central vein thrombosis and a man aged 57 presented closed angle glaucoma with associated glaucomatous field *loss despite surgical treatment Of the* patients with originally normal conditions only three (three eyes) developed glaucomatous field loss Their case histories will be briefly reported

Case reports 1 (case 256/61 67) A man aged 68 with a screening tension of 26 mm Hg of both eyes Ophthalmoscopy (including retinal photo) and visual field measurements showed normal conditions All the control pressure values measured were 25 mm Hg or higher Water provocative test released a rise from 21 mm Hg to 31 mm Hg in the right eye but no pathological rise in the left The priscol provocative test was *negative* in both eyes Treatment was instituted with a resulting pressure level of 20–21 mm Hg of both eyes within the observation period The follow up examination disclosed a definitely glaucomatous optic disc in the *right eye but unchanged normal conditions* in the left Visual field measurement had to be given up owing to failing co operation Conclusion development of glaucoma with field loss in the right eye

2 (case 141/61 67) A woman aged 6 with a screening tension of 27 mm Hg of the right eye and 18 mm Hg of the left In the right eye ophthalmoscopy (including retinal photo) and visual field measurement showed normal conditions Several control pressure measurements gave values of 25 mm Hg or higher Water provocative test re

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leased a rise from 26 mm Hg to 34 mm Hg No priscol provocative test was made The condition of the left eye could not be assessed owing to cataract. All the control pressure values measured were below 20 mm Hg and the water provocative test gave a negative result Treatment was instituted of the right eye. The pressure level was 25 mm Hg or higher during the observation period In the left eye the intra ocular pressure remained below 20 mm Hg without treatment The follow up examination showed in the right eye a definitely glaucomatous disc and visual field measurement revealed an arcuate scotoma superiorly with peripheral break through and defects in the upper nasal quadrant In the left eye the condition was still impossible to assess owing to cataract Conclusion development of glaucoma with field loss of the right eye

3 A woman aged 70 with screening tensions of 19 mm Hg (right eye) and 21 mm Hg (left eye) Ophthalmoscopy and visual field measurement showed normal conditions The water provocative test released a rise from 19 mm Hg to 24 mm Hg in the right eye and from 21 mm Hg to 27 mm Hg in the left eye No priscol provocative test was made Control pressure measurements gave 20–21 mm Hg Treatment was instituted after two years The pressure level was 20–21 mm Hg during the observation period On the follow up examination both discs were characterized as glaucoma suspicious Visual field measurement revealed arcuate scotoma superiorly with no peripheral break through in the right eye and a normal visual field in the left Conclusion development of glaucoma with field loss of the right eye

Provocative tests An evaluation on the basis of the present investigation of the chances the provocative tests may have of prognosticating the further course must in any case be accepted with a certain reservation but is in particular interfered with by possible alterations caused by the therapy instituted

Considering with this reservation the patients who developed glaucomatous field loss despite treatment and who had a water provocative test carried through we found a pathological rise ($\geqq$ 8 mm Hg) in no more than three out of 11 eyes

Another question suggesting itself in this connection is whether the result of the water provocative test may predict a rise of the tension to a pathological level – in this study set arbitrarily at 25 mm Hg Among the patients characterized as borderline cases and patients with untreated glaucoma such a situation without glaucomatous field loss was present in seven (11 eyes) and five (7 eyes) respectively Only three out of these 18 eyes showed a pathological rise

Estimated on the basis of these findings the water provocative test seemed to give no indication of the further course neither for the patients presenting an additional field loss at the follow up nor for the patients who developed a pressure level of 25 mm Hg or higher during the observation period

The priscol provocative test could not be assessed on the same lines owing to the small number of tests available

The course among the 110 followed up patients considered in relation to classification in glaucoma cases borderline cases and normals The object of this assessment was to get an impression of the extent to which the original classification could be maintained after five years In this connection we must bear in

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ROUTINE TONOMETRY IN OPHTHALMIC PRACTICE

II Five Year Follow Up

BY

KNUD NØRSKOV

The desire for an intensification of the glaucoma prophylactic work by means of routine tonometry is based primarily on the fact that using the traditional form of glaucoma tracing the disease has in fact been found to be among the three most frequent causes of blindness (Rapp epidem demogr 1966 Nørskov 1968)

Furthermore it is a common clinical impression that the prognosis of simple glaucoma traced before field loss has set in is considerably more favourable than that of glaucoma at an advanced stage However only few comprehensive investigations all retrospective are available in support of this impression as mentioned by Leydhecker 1960a Dake 1967 and Leopold 1967 among others

Moreover employment of routine tonometry in the glaucoma prophylactic work requires that it is possible by tonometry to single out the persons who later will develop visual field defects in accordance with the hypothesis advanced by Leydhecker (1959) and Goldmann (1959) that the ocular hypertension precedes the visual field defects by 15–18 years

However in spite of a very considerable number of glaucoma screenings carried through only few reports on follow up examinations are available by which to assess the further course in cases traced by routine tonometry

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mind however that a possibly modified characterisation was based solely on ophthalmoscopic and visual field alterations and on alteration of the pressure level the follow up examination having not included provocative tests

In conformity with the previously chosen criteria a pressure level below 20 mm Hg was characterized as normal a pressure *level of 20–24 mm Hg* as a borderline range and 25 mm Hg or higher as an arbitrarily chosen pathological level

The classification of the 110 patients followed up is shown in table 1 50 patients had glaucoma of one or both eyes 48 patients were characterized as borderline cases and 12 patients as normal

Glaucoma The age and sex distribution is seen in table 1 Of the 50 patients 13 had remained untreated while 37 (72 eyes) had received antiglaucomatous drug treatment in seven cases (12 eyes) supplemented by surgical intervention

Table 4 *renders pressure levels for the 37 patients (72 eyes) subjected to treatment. It is seen that a regulation of the tension to below* 20 mm Hg *was obtained in no more than 14 eyes*

In 29 patients no glaucoma provoked alteration was noticed of central visual acuity ophthalmoscopic findings or visual field

Eight patients (11 eyes) presented progression of the glaucoma Two of these showed central vein thrombosis as well of one eye while in two other cases (two eyes) the disease had developed from previously normal conditions (cases 1 and 2)

The other four patients (six eyes) showed progression of existing visual field defects

In six patients improvement of the state was observed In five of these (six eyes) as stated above *a previously noticed baring of the blind spot was not re*

Table 4

Pressure level during the observation *period in 50 patients (98 eyes)* characterized as glaucoma cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	6	14	20
20–21 mm Hg	3	20	23
22–24 mm Hg	6	29	35
≥ 25 *mm Hg*	11	9	20
Total	6	72	98

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producible and in one the extent of the visual field defects became reduced after a cataract operation

Table 4 also shows the pressure levels in the 13 untreated cases It is seen that in two thirds of the cases (17 eyes) the pressure level was 22 mm Hg or higher In spite of this none of the untreated glaucoma patients displayed any glaucoma provoked alterations of visual field and ophthalmoscopic findings

Of the 12 patients with fairly advanced glaucoma at the time of the primary screening, seven (10 eyes) were followed up Additional progression was recorded in half of these eyes despite treatment and a pressure level of 20–24 mm Hg while in the other half the conditions had remained unchanged In two of the latter eyes the pressure level was above 25 mm Hg All in all these findings stress the bad prognosis for eyes presenting a rather extensive glaucomatous field loss

Glaucoma according to the chosen criteria was unilaterally present in ten of the patients followed up Six of these had both eyes treated Only a single patient had developed visual field defects of the non glaucomatous eye

Borderline cases The age and sex distribution of 48 patients is seen in table I

43 patients remained untreated during the observation period and visual field measurement and ophthalmoscopy revealed no glaucomatous changes in these cases An altered characterisation in keeping with the stated criteria must therefore be based solely on the pressure values during the observation period

It is shown in table 5 that during the observation period pressure levels below 20 mm Hg were recorded in 17 eyes without treatment but only in four patients in both eyes In conformity with the criteria employed these latter borderline cases should be characterized as normal after the follow up

Table 5 also shows that during the observation period pressure levels of 25 mm Hg or higher were recorded for four eyes (three patients) These eyes all

Table 5

Pressure level during the observation period in 48 patients (96 eyes) characterized as borderline cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	17	1	18
20–21 mm Hg	38	4	42
22–24 mm Hg	27	5	32
≥ 25 mm Hg	4	–	4
Total	86	10	96

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Furthermore it is a common clinical impression that the prognosis of simple glaucoma traced before field loss has set in is considerably more favourable than that of glaucoma at an advanced stage However only few comprehensive investigations all retrospective are available in support of this impression as mentioned by Leydhecker 1960a Dake 1967 and Leopold 1967 among others

Moreover employment of *routine* tonometry in the glaucoma prophylactic work requires that it is possible by tonometry to single out the persons who later will develop visual field defects in accordance with the hypothesis advanced by Leydhecker (1959) and Goldmann (1959) that the ocular hypertension precedes the visual field defects by 15–18 years

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presented a rise from 22–24 mm Hg to maximally 27 mm Hg The three cases should accordingly be characterized as having changed from borderline cases to glaucoma cases but as stated without glaucomatous *field loss*

Five patients had treatment instituted after a pressure level of 25 mm Hg or higher had been recorded within the observation period It is seen in table 5 that despite *treatment regulation* of the tension to below 20 mm *Hg* was obtained in a single case only One patient (case 3) with previously normal conditions had developed visual field defects while another with originally glaucoma suspicious discs had developed distinct marginal cupping of the optic discs where visual field measurement could not be carried through

The over all result of the follow up examination of 48 patients primarily characterized as borderline cases was that for eight the characterisation had to be altered to glaucoma though only in two cases with glaucomatous field loss while four were to be characterized as normal

Normals Table 1 shows the age and sex distribution of 12 patients characterized as normal after further examinations Neither visual field measurement nor ophthalmoscopy revealed any glaucoma provoked alterations and seven patients had unaltered pressure values below 20 mm Hg Five patients had pressure values of 20–21 mm Hg recorded These should therefore according to the chosen criteria be transferred from the group of normals to that of borderline cases However the shifts of tension values are seen to have been small

Assessment of the further course among the 110 patients followed up considered in relation to alterations of the screening level In the endeavours to reduce by routine tonometry the number of patients referable to further examination we aimed on the primary screening at getting an impression of the relation between an alteration of the screening level and the number of missed glaucoma cases We proceeded by raising the screening level to ≥ 21 ≥ 22 and ≥ 25 mm Hg respectively together with a graduation according to age Thus the screening level was altered to 22 mm Hg or higher *for patients aged between* 35 and 64 and to 25 mm Hg or higher for patients aged over 65 The stated alterations of the screening procedure effected as might be expected a reduction of the number of patients referable to further examination but at the expense of missed glaucoma cases judged from the criteria chosen (Nørskov 19 0b)

It will therefore be valuable to have the further course clarified for the patients missed owing to the *respective alterations* of the *screening level* to be able to estimate which alterations might be warranted

A rise of the screening level to 21 mm Hg at the primary screening would have effected that 38 of the 110 patients followed up had not been suspected of glaucoma on routine tonometry Four of these patients characterized as having glaucoma were treated without obtaining a pressure level below 20 mm Hg None of the 38 patients developed visual field defects within the observation

The results of the follow up examinations carried out go to show that routine tonometry contributes towards intensifying the glaucoma tracing work (Leydhecker 1960b 1966) and at the same time that employment of tonometry is of limited value as an aid to singling out the persons who later will develop glaucoma with field loss (Linner & Stromberg 1964 1967, Becker & Morton 1966 Armaly 1969 Nørskov 1970a)

Investigations with a view to assessing the further course among normals have been undertaken by Armaly (1960 1962 1969) Linner & Stromberg (1967) and in previous studies by the author (Nørskov 1967, 1970a)

In the present paper the results will be reported of a five year follow up performed in relation to applanation tonometry carried out as a routine among patients in ophthalmic practice

The investigation comprised follow up examination and assessment of the course in the patients suspected of glaucoma after routine tonometry Further the investigation included assessment of the course based on information given by the only ophthalmologist of Falster regarding the patients who after applanation tonometry had been characterized as normal

Own Material

In a previous paper (Nørskov 1970b) the results are reported of routine tonometry among patients aged over 35 on the Island of Falster who consulted the only ophthalmologist of Falster within the period from October 1 1960 to February 28 1962

Among the 1882 patients subjected to applanation tonometry 169 (9 0 per cent) had an intra ocular pressure of 20 mm Hg or higher recorded

Establishment of the glaucoma diagnosis required presence of one or more of the following criteria 1 distinct marginal cupping of the optic disc 2 reproducible glaucomatous visual field defects 3 pressure values ≧ 25 mm Hg 4 rise ≧ 8 mm Hg in response to water provocative test 5 rise ≧ 11 mm Hg in response to priscol provocative test. 6 rise ≧ 8 mm Hg in response to mydriasis test 7 rise ≧ 10 mm Hg in response to darkroom test

75 patients had the glaucoma diagnosis established in one or both eyes while 78 were characterized as borderline cases and 16 as normal

After the examination with a view to tracing glaucoma another ten patients were regarded as suspects despite a screening tension below 20 mm Hg However none of these later had the glaucoma diagnosis established

1703 patients were characterized as normal after routine tonometry

A five year follow up was carried through in November and December 1966 an out patient follow up examination having been arranged in the ophthalmic

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Table 4 also shows the pressure levels in the 13 untreated cases It is seen that in two thirds of the cases (17 eyes) the pressure level was 22 mm Hg or higher In spite of this none of the untreated glaucoma patients displayed any glaucoma provoked alterations of visual field and ophthalmoscopic findings

Of the 12 patients with fairly advanced glaucoma at the time of the primary screening seven (10 eyes) were followed up Additional progression was recorded in half of these eyes despite treatment and a pressure level of 20-24 mm Hg while in the other half the conditions had remained unchanged In two of the latter eyes the pressure level was above 25 mm Hg All in all these findings stress the bad prognosis for eyes presenting a rather extensive glaucomatous field loss

Glaucoma according to the chosen criteria was unilaterally present in ten of the patients followed up Six of these had both eyes treated Only a single patient had developed visual field defects of the non glaucomatous eye

Borderline cases The age and sex distribution of 48 patients is seen in table 1

43 patients remained untreated during the observation period and visual field measurement and ophthalmoscopy revealed no glaucomatous changes in these cases An altered characterisation in keeping with the stated criteria must therefore be based solely on the pressure values during the observation period

It is shown in table 5 that during the observation period pressure levels below 20 mm Hg were recorded in 17 eyes without treatment but only in four patients in both eyes In conformity with the criteria employed these latter borderline cases should be characterized as normal after the follow up

Table 5 also shows that during the observation period pressure levels of 25 mm Hg or higher were recorded for four eyes (three patients) These eyes all

Table 5

Pressure level during the observation period in 48 patients (96 eyes) characterized as borderline cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	17	1	18
20–21 mm Hg	38	4	42
22–24 mm Hg	27	5	32
≥ 25 mm Hg	4	–	4
Total	86	10	96

clinic, *Centralsygehuset* Nykøbing Falster including both the 169 patients whose screening tension had been measured at 20 mm Hg or higher and the ten other patients suspected of glaucoma after the screening

A five year assessment of the course for the 1,03 patients characterized as normal after routine tonometry was based solely on data from the case records of the only ophthalmologist of the island

1 Follow Up of the Patients who at Routine Tonometry had a Screening Tension of 20 mm Hg or higher

Of the 169 patients 46 had died within the observation period while in the cases of 13 patients a five year follow up examination could not be carried through for different reasons

The number of patients subjected to a five year follow up examination was thus reduced to 110 of whom 42 were under treatment while 68 were untreated

A. Patients Subjected to a Five-Year Follow Up

This group comprised as stated 110 patients practically all examined in the Department of Ophthalmology *Centralsygehuset* Nykøbing Falster 104 by the author in person These patients represented 65 per cent of the original 169 found to have an intra ocular pressure of 20 mm Hg or higher

The follow up examination included determination of the central visual acuity ophthalmoscopy campimetry (preferably object sizes 2/2000 and 6/2000) and applanation tonometry The examinations were performed at different times of the day according to the desires of the individual patients

Where possible the examination was supplemented by data from the oph thalmic consultations within the observation period The number of control examinations by the ophthalmologist varied considerably While thus 35 patients (32 per cent) failed to attend for control among whom however only three with a diagnosis of glaucoma 45 patients had attended from 10 to 56 times

Though we must reckon with failing attendance for control by some of the patients – in the present series one third – the survey of the number of control consultations within the observation period illustrates the great work with which the ophthalmologist going in for routine tonometry is nevertheless burdened

The age and sex distribution of the 110 patients followed up is shown in table 1 26 were males and 84 females The youngest patient was 41 years old and the oldest 86 (average age 66)

Table 1 also illustrates the distribution according to diagnosis It is seen that 50 cases were diagnosed as glaucoma while 48 were characterized as borderline cases and finally 12 as normal

gression One patient with previously normal conditions who failed to appear for control developed visual field defects

C Patients Dead Within the Observation Period

46 patients died within the observation period These constituted 27 per cent of the 169 subjected to further examination The mortality was 60 per cent for patients aged over 75 Half of the 46 patients had died before the elapse of three years The relatively few data available must be considered in assessing the course in this group Half of the patients had it is true, consulted an ophthalmologist less than six months before death but 13 had not been seen for control

Four patients under treatment who had glaucoma at an advanced stage presented with a single exception further development of their visual field defects and one patient had become blind of both eyes To judge from the data available none of the other patients had shown any glaucoma provoked changes of the state

D Further Course in Patients Aged Over 75

As stated above a considerable number of the patients aged over 75 had died within the observation period A separate assessment was therefore desirable of the conditions in the 42 patients aged over 75 at the time of the screening It appeared that 25 patients had died Five could not be followed up while 12 were subjected to follow up examination

Of the 42 patients 14 had been under treatment but only in two cases with a resulting regulation of the tension to below 20 mm Hg Five patients under treatment and with glaucomatous field loss presented further progression of the disease In one case glaucomatous field loss was seen in a patient with originally normal conditions (case 2)

E Development of Blindness Within the Observation Period

Of the 110 patients followed up two – males aged 50 and 74 respectively – had become blind within the five year observation period according to the definition of blindness indicated by the Danish Society for Blind Welfare (a visual acuity not exceeding 4/60 or a visual field below 20° and combinations of these defects) These patients both had central vein thrombosis in addition to glaucoma

Among the 46 patients dead within the observation period further information on development of blindness was available in three cases In only one of these – a woman aged 87 – was the blindness due to glaucoma One of the other

Table 1

Age and sex distribution and characterisation of 110 patients followed up

age	glaucoma diagnosed		borderline cases		normals		Total	
	males	females	males	females	males	females	males	females
35–44	–	–	1	3	–	1	1	4
45–54	2	2	4	5	–	2	6	9
55–64	6	6	–	11	–	2	6	19
65–74	5	13	3	11	1	4	9	28
75–84	1	11	1	7	–	2	2	20
≥ 85	1	3	1	1	–	–	2	4
Total	15	35	10	38	1	11	26	84

Results

In assessing the results there is reason to concentrate in the first place on the question of the chances the individual methods of examination have of prognosticating the further course

Anamnestic data On the primary tracing we tried to single out a group among the patients subjected to further examination on the basis of our knowledge concerning a relationship between glaucoma and central vein thrombosis glaucoma and diabetes glaucoma and high myopia glaucoma and thyroid dysfunction and glaucoma and pseudoexfoliation (Becker & Shaffer 1965) Of the 25 patients constituting this group only 12 had follow up examination carried through 12 had died within the observation period among whom nine out of 12 with diabetes mellitus This is a factor to be considered together with the patient s age when deciding on the extent of the further examinations and possible institution of treatment of diabetics

Of the 12 patients followed up nine had glaucoma for which they had been treated during the observation period Progressive glaucoma occurred in two out of four patients with combined central vein thrombosis and glaucoma The others showed no change

Seven out of eight patients who gave information on a familial predisposition were subjected to follow up examination Five patients under treatment had glaucoma of whom four with greater or smaller visual field defects Progression of the glaucoma during the observation period was noticed in one case only

To judge from the present investigation information on a familial predispo

period and only one had an alteration recorded of the pressure level to 25 mm Hg or higher One patient who presumably would have been caught by presence of glaucoma suspicious optic discs showed unaltered beginning visual field defects

By raising the screening level to 22 mm Hg 60 patients would not have been suspected of glaucoma on routine tonometry Ten patients were treated during the observation period but only half obtained regulation of the tension to below 20 mm Hg Four of the treated patients presented visual field defects Two of these had developed a more advanced glaucoma In four untreated patients a rise of the pressure level to 25 mm Hg or higher was recorded In 52 cases the state had remained unchanged

By raising the screening level to 25 mm Hg 81 of the 110 patients followed up would not have been suspected of glaucoma 17 of these were treated during the observation period with a resulting fall of the pressure level to below 20 mm Hg in five Visual field defects were seen in six of the treated patients of whom four presented glaucoma at an advanced stage Seven untreated patients had rises of the pressure level to 25 mm Hg or higher recorded 68 of the 81 patients displayed no glaucoma provoked changes of the state

By raising the screening level to 22 mm Hg for patients ranging in age from 35 to 64 a total of 41 patients would not have been suspected of glaucoma on routine tonometry Eight patients were subjected to treatment of whom two had the tension regulated to below 20 mm Hg None of the 41 patients had developed visual field defects within the observation period One of those not treated had a rise of the pressure level to 25 mm Hg or higher recorded One patient who presumably would have been caught by presence of glaucoma suspicious optic discs displayed unaltered beginning visual field defects

If the screening level had been raised to 25 mm Hg for patients over 65 years of age 27 of the patients followed up would not have been suspected of glaucoma on routine tonometry Five of these patients had been treated with the result that two had obtained a regulation of the tension to below 20 mm Hg Among the treated patients four displayed visual field defects of whom two had glaucoma at a fairly advanced stage In two patients subjected to no treatment the pressure level recorded had risen to 25 mm Hg or higher In the remaining 21 of these 27 patients no change of the state due to glaucoma was noticed

B Patients Not Subjected to a Five Year Follow Up

In the cases of 13 patients follow up examination could not be carried through from different causes In general only few data were available for this group Two patients had therapy instituted with a resulting regulation of the tension to below 20 mm Hg but in only one of these was it possible to prevent pro

sition and occurrence of central vein thrombosis are the factor of the greatest value in tracing glaucoma

Pressure level Table 2 shows a recording of the pressure levels during the observation period for all the 110 patients (220 eyes) based on measurements at the follow up supplemented by measurements carried out by the ophthalmologist within the observation period Of the 110 patients 68 were untreated while two had only one eye treated

Among the 68 patients a pressure level of 22 mm Hg or higher was recorded for 46 eyes or 33 3 per cent

Among 42 patients who had treatment instituted a pressure level below 20 mm Hg was obtained for no more than 15 eyes (18 3 per cent) while in half of the cases (52 4 per cent) levels of 22 mm Hg or higher were recorded

In table 3 the pressure levels recorded on the further examination in the ophthalmic unit following the original examination is compared with the levels found at the follow up for 68 patients (136 eyes) given no treatment It is seen that in 67 eyes (49 3 per cent) the pressure level was unaltered A lower level was recorded for 15 eyes (11 0 per cent) However only two obtained a fall from 25 mm Hg or higher to within the range of 20–24 mm Hg and only one a fall from 25 mm Hg or higher to below 20 mm Hg

A higher pressure level at the follow up was recorded for 54 eyes (39 7 per cent) but only nine showed a rise from the 20–24 mm Hg range to 25 mm Hg or higher and in only a single case was a rise noticed from below 20 mm Hg to 25 mm Hg or higher

The pressure values compared originating from single measurements which need not have been carried out at the same time of the day the conclusions we may be justified in drawing are limited Evidently however no definite change towards a higher pressure level occurred during the observation period Similar shifts towards both higher and lower pressure values as in the present series have been recorded by Linner & Stromberg (1964) Leydhecker (1966) and the

Table 2
Pressure level during observation period in 220 eyes (110 patients)

	< 20 mm Hg	20–21 mm Hg	22–24 mm Hg	≥ 25 mm Hg	Total
without treatment	41	51	31	15	138
with treatment	15	24	34	9	82
Total	56	[illegible]	65	24	220

Table 6

Age and sex distribution of 222 previously normal patients who had their intra ocular pressure measured on consulting the ophthalmologist within the observation period

age	males	females	Total	pressure level					
				20–21 mm Hg		22–24 mm Hg		≥ 25 mm Hg	
				males	females	males	females	males	females
35–44	9	32	41	1	–	–	–	–	–
45–54	23	68	91	1	6	–	–	–	–
55–64	9	44	53	–	5	2	4	–	2
65–74	6	26	32	4	5	–	2	–	1
75–84	3	2	5	–	2	–	–	–	1
Total	50	172	222	6	18	2	6	–	4

The 2nd Department of Ophthalmology of the Medical School Budapest
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CANALICULOPLASTY

BY

IMRE KORCHMÁROS

This is a brief report on some of our procedures for lacerated or obstructed lacrimal canaliculus

The procedures were mostly performed in block anaesthesia

In cases of lacerated canaliculi if the torn end of the nasal stump is invisible a few drops of fluid (e g adrenaline chloramphenicol eye drops) are dropped into the wound and the patient is asked to blow out air through the nose while his nostrils are compressed As it is well known to everybody sometimes air bubbles appear in the fluid (1 2) indicating the torn end of the nasal stump If they do not air is injected from a syringe through the intact canaliculus Obviously the lower part of the lacrimal sac must be blockaded by a suitable blunt tool pressed onto the skin (Fig 1) as it is made at retrograde irrigation for canaliculitis (3)

The so called retrograde procedure can also be performed by using the retrograd cannula (4) This spiral formed canule (Fig 2) is introduced from the intact canaliculus into the lacerated one Thus air or fluid can be injected directly into the lacerated canaliculus in order to find the torn end (Fig 3) The syringing itself makes it easier to drive the retrograd cannula

The retrograd cannula may be used simultaneously for the reconstruction too After a few rotations the tip of the canule appears in the torn end of the lacerated canaliculus Then a plastic thread is inserted into the canule (Fig 4) the instrument is withdrawn the thread is inserted into the temporal

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two patients had become blind owing to senile macular degeneration and the other to proliferative diabetic retinopathy

Blindness was thus recorded for five patients but in one case only was glaucoma the sole cause of this

II Follow Up of Patients Suspected of Glaucoma Despite a Screening Tension Below 20 mm Hg

This group comprised ten patients, of whom seven were followed up In agreement with the results of the original further examinations no signs of glaucoma were seen in this group consisting mainly of patients who on routine tonometry had shown a difference exceeding 4 mm Hg between the right and the left eye

III Course in the Patients Characterized as Normal on Routine Tonometry

1703 patients were characterized as normal on the basis of routine tonometry For this group a five year follow up was impossible to carry through An attempt was made instead to judge of the further fates of these patients by utilizing the data procurable from the case records of the only ophthalmologist of Falster

These showed that 538 of the 1703 patients (32 per cent) had consulted the ophthalmologist within the observation period Similarly as noted for the routine tonometry the number of females attending for renewed examination exceeded that of males being 36 per cent (389 females) and 24 per cent (149 males) respectively The age distribution was fairly uniform though with the lowest representation of the age groups of 35–44 and 75–84

The patients were examined in accordance with the causes of their consulting the ophthalmologist Ophthalmoscopy showed normal optic discs in all cases On the examination no special point was made of having the intra ocular pressure recorded again Therefore (table 6) anly 222 patients (50 males and 172 females) corresponding to 41 per cent of those attending or 13 per cent of the original 1703 patients were subjected to renewed applanation tonometry

Table 6 shows the age and sex distribution of 36 patients who had an intra ocular pressure of 20 mm Hg or higher recorded within the observation period The mean age at the time of control pressure measurement was 61 the youngest patient being 44

The incidences of pressure values $\geqq$ 20 mm Hg $\geq$ 22 mm Hg and $\geq$ 25 mm Hg were 16 2 per cent (36 patients) 5 4 per cent (12 patients) and 1 8 per cent (4 patients) respectively The highest intra ocular pressure recorded was 27 mm Hg No patient aged under 55 had an applanation value of 22 mm Hg or higher measured

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THE EFFECT OF TRACHOMA ON INTRAOCULAR TENSION

BY

P AWASTHI and R P S BHATIA

Trachoma as a source of human suffering a cause of blindness and as such causing economic loss over large tracts of the World is second to none amongst the diseases of the eye or indeed diseases of all kinds

It is a specific contagious disease of chronic nature the course of which is prolonged and the tendency towards gradual healing by fibrosis is almost a uniform feature Taking this fibrosis into view some workers have reported in favour of a relationship between trachoma and ocular hypertension Investigators like *Wecker* (1900) *Mc Callen* (1936) *Sedan* (1939) and *Boles Carenini* & *Combiaggi* (1957) have shown that the frequency of glaucoma is definitely higher in trachomatous subjects than among non trachomatous On the other hand *Guarino* (1914) *Lagrange* (1922 *Terson* (1928) *Trantas* (1937) and *Pasion* (1957) advocate that the two conditions are independent However the factor of scleral rigidity has not been taken into account by these workers and higher rigidity might have given rise to erroneous diagnosis of glaucoma Hence 141 cases of trachoma were subjected to tonometry Moreover scleral rigidity was also derived firstly to assess the effect of trachoma on ocular rigidity and secondly to avoid false tonometric conclusions

Material and Methods

The patients for the present study were those attending the department of Ophthalmology S N Medical College Agra These cases were either suffering from trachoma or had suffered from trachoma

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bers of the donor corps of Falster traced by applanation tonometry (Norskov 1970a) Further they are supported by more summary statements based on follow up examinations by Bertelsen (1965) Norskov (1967) Fruhauf *et al* (1968) and Graham (1968)

The assessment is more difficult where the treated patients are concerned Of the 42 treated patients showing normal conditions at the primary screening only three developed glaucomatous field loss (cases 1–3 pp 879–880) These ranged in age from 68 to 76 at the time of the primary screening In one of these patients the screening tension of the eye concerned was 19 mm Hg being thus below the screening level This patient had been caught by a screening tension of 21 mm Hg of the opposite eye

A similar problem regarding treated and untreated patients subjected to follow up examination presented itself in the follow ups carried out by Leydhecker (1960b 1966) after three and seven years respectively A comparison of the results achieved may be of interest though the patients were selected constituting groups from ophthalmic practice and employees of a business respectively

It is remarkable that Leydhecker (1960b) on a follow up examination of glaucoma patients after three years of observation recorded glaucomatous field loss in 32 5 per cent of those with previously normal visual fields The present investigation showed such a development in no more than 7 per cent of the treated patients and in none of the untreated

In assessing the course in the treated patients we must bear in mind that of course the treatment can only be expected to have effect if it really does bring about a fall of the pressure A regulation to below 20 mm Hg is supposed to be required (Weekers *et al* 1959 Goldmann 1960 Lawætz 1960 Touvinen 1961 Leydhecker 1963 Shaffer 1967 Sugar 1969)

It has however been noticed often to be difficult to obtain a fall in eyes with a pressure level about 25 mm Hg which in fact will predominate among patients traced on examinations for revealing glaucoma (Goldmann 1960 Walker 1966 Leopold 1967)

In agreement with this the present investigation showed that an ideal normalisation to below 20 mm Hg was obtained in no more than 18 per cent of the treated eyes while a pressure level of 22 mm Hg or higher was present in 52 per cent Progression of the visual field defects was seen in 17 per cent (14 eyes) of the total number treated

Leydhecker (1966) at the follow up after seven years likewise recorded pressure levels of 22 mm Hg or higher in two thirds of treated or untreated glaucoma cases whereas progression of visual field defects was noticed in 40 per cent of the total number of glaucoma cases

A comparison of the two materials is actually unrealistic If nevertheless one will attempt to give a possible explanation of the considerable difference between the assessments of the further course for patients traced by routine

The clinical examination of both the eyes was done firstly by oblique illumination and then by the slit lamp The main aim was to examine the lids for any sequelea of trachoma conjunctiva for follicles and scarring and lastly cornea for pannus scarring and opacities etc

On the basis of above examination the patients were categorised according to the W H O classification of trachoma

As a control case 51 medical students of both the sexes were examined who were free from trachomatous infection clinically

The intraocular pressure of these patients was recorded by paired tonometry to establish the scleral rigidity in addition to the ocular tension

Observations

A total of 141 cases belonging to various stages of trachoma were examined The age of these patients were between 15 to 40 years which is presumably the preglaucoma age

Fig 1 shows the stages of trachoma and the age group of the 141 patients of the present study

The intraocular tension above 22 mm Hg in eight patients (5 67 %) mostly belonging to IV stage defintely categories these patients into *suspicious group of glaucoma cases* which alarms for a thorough checking and constant super vision time to time

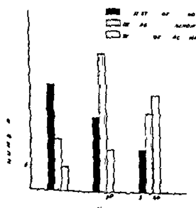


Fig 1
Showing cases of various age groups in different stages of trachoma

On the basis of the data available and referring to the criteria chosen a diag nosis of glaucoma but without field loss was established in two women aged 62 and 64 respectively In the other two cases in which a pressure value of 25 mm Hg or higher had been measured within the observation period control measurements gave a pressure level below 25 mm Hg

Discussion and Conclusion

Through the present investigation it has been aimed at giving the best possible illustration of the further course during a five year observation period within a group of patients aged over 35 who had consulted an ophthalmic medical practitioner This group comprised 169 patients with an intra ocular pressure of 20 mm Hg or higher 10 patients whose condition also raised suspicion of glaucoma and finally 538 patients characterized as normal who re consulted the ophthalmologist within the observation period

Of the 169 patients 110 or 65 per cent were followed up while 46 had died within the observation period and 13 could not be followed up for different reasons

A very important question in a follow up of this kind is that of the course with out treatment in a group of patients suspected of glaucoma after routine tono metry

No direct answer can be given to this question on the basis of the present in vestigation For ethical reasons the ophthalmologist had to offer treatment when the glaucoma diagnosis had been established according to the chosen criteria In addition at the time of the primary screening treatment of patients without glaucomatous field loss was insisted on (Schmidt 1960 Leydhecker 1960b 1963)

Of the 110 patients followed up 42 were consequently under treatment and 68 untreated

Among the 68 untreated patients none had developed glaucomatous field loss during the observation period The extent of the visual field defects had remained unchanged in one patient

To judge from the course in the 68 untreated patients the chance that pa tients with a mild ocular hypertension will develop glaucomatous field loss within a five year period seems to be small This is in agreement with the views previously advanced by Linnér & Strömberg (1964 1967) based on follow up examinations after two and five years of untreated persons with ocular hyper tension These results are borne out by those of follow up examinations car ried through by Haas (1967) and Armaly (1969) and those of a five year fol low up performed by the author on the same lines as the present among mem

The values of corrected tension and the coefficient of scleral rigidity were expressed according to the table of Becker & Shaffer

These patients were put into the following groups on the basis of corrected tension

1 Group A – Patients with the tension above 22 mm Hg
2 Group B – Patients between the tension 19 21 mm Hg
3 Group C – Patients with a tension below 19 mm Hg

Fig 2 shows the distribution of the cases into these various groups –

Discussion

In severe cases of trachoma and especially in repeated reinfection the whole circumference of the cornea becomes vacularised infiltrated and finally scarred Implication of the aqueous veins in the trachomatous infiltrative process or worse still in the trachomatous scarring of the limbic and paralimbic regions might lead to an impediment to the outflow of aqueous humour and a consequent rise of the intraocular pressure

As described 141 cases of trachoma were subjected to paired tonometry The coefficient of scleral rigidity and the intraocular tension were expressed according to the table of Becker & Shaffer

It was observed that out of 141 cases 8 patients (5 67 %) showed a definite *rise of tension above 22 mm Hg The mean value of tension* was 24 25 with

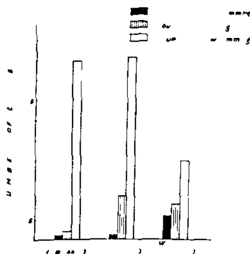


Fig 2
Showing intraocular tension in various stages of trachoma

velopment of visual field defects were noticed in ten patients (14 eyes) Seven of these would however probably have been caught by ophthalmoscopy presence of central vein thrombosis or elucidation of a familial predisposition a circumstance which stresses the importance of these factors in glaucoma tracing On the other hand to judge from the results of the present investigation the water provocative test yielded no prognostic suggestions neither for patients displaying additional glaucomatous field loss during the observation period nor for patients with a rising pressure level to an arbitrarily chosen pathological value of 25 mm Hg or higher in the course of the observation period The same impression that the water provocative test has a very limited possibility of prognosticating the further course has been stated by Armaly (1969) and by the author on the basis of a previous follow up study (Nørskov 1970a)

It would be well if the results of the present investigation might serve to suggest a modification of the screening procedure so as to reduce the number of patients suspected of glaucoma and at the same time facilitate encircling of patients being particularly liable to develop visual field defects In the present investigation similarly as at the primary screening it was chosen to study the consequences of altering the screening level to ≥ 21 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg respectively and to undertake a graduation according to age using a screening value of 22 mm Hg or higher for the age group of 35–64 and 25 mm Hg or higher for that over 65

Reservation must in any case be made with regard to reflections of this kind with a view to suggestions for altering the glaucoma screening procedure on the basis of a limited series of patients The problem to be considered is in fact that of the margin of security with which one desires to work within the field of glaucoma screening provided one attributes a central position to routine tonometry If we may be justified in drawing certain conclusions on this basis it seems that choice of 21 mm Hg as the screening level may be permissible This has in fact often been indicated as an appropriate screening level when applanation tonometry is employed (Goldmann 1960 Schmidt 1960 Becker & Shaffer 1965 Chandler 1965 Leopold 1967 Pollack 1967)

The results of the present investigation also suggest that a screening level of 22 mm Hg might be considered for patients ranging in age from 35 to 64 On the other hand the remaining suggestions for altering the screening level probably cannot be insisted on without definitely departing from the fundamental principles of routine tonometry

Another possibility of improving the screening procedure might be based on the fact that 60 per cent of the patients aged over 75 had died within a five year period A review of this group disclosed that all the patients presenting further development of glaucoma during the observation period also had had glaucomatous or glaucoma suspicious optic discs recorded on the primary screening However at the same time it was noticed that one of the three patients who

standard deviation of 0 75 This rise in ocular pressure was statistically significant (0 001 < 0 005) The maximum number (6) of these patients belonged to IV stage of trachoma and only one case of II stage and one case of III stage (Fig 2) The maximum rise of tension in as many as six cases in IV stage suggests that fibrosis and scarring in this stage plays a vital role to make the eye prone to be hypertensive It has been suggested that trachomatous scarring hinders in the outflow of aqueous presumeably affecting the aqueous veins

In cases of IV stage of trachoma there was an apparent rise in coefficient of rigidity with an average of 0 0234 and a standard deviation og 0 0072 But statistically this change was insignificant (0 001 < 0 005) (Fig 3)

?? cases (15 60 %) out of 141 patients presented with a tension between 19 to 21 mm Hg (Average 19 77 and standard deviation 1 04) In these cases the ratio was higher in IV stage of trachoma The coefficient of scleral rigidity in these cases was within normal limits statistically (average 0 0232 standard deviation 0 071)

Rest 111 cases present with an ocular tension below 19 mm Hg (average 14 97 and standard deviation 2 91) Their mean ocular rigidity was 0 0225 (standard deviation 0 0069) which was normal statistically

In control group the mean intraocular tension was 14 41 mm Hg (Standard deviation 4 6) and the mean value of ocular rigidity was 0 0227 (standard deviation 0 0068)

It is suggested therefore that the tension must be recorded in all the cases with trachoma especially in late stages to discover unsuspected cases of glaucoma

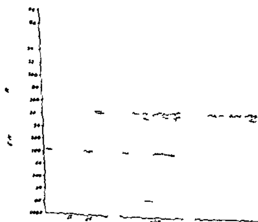


Fig 3
Scattergram showing distribution of scleral rigidity in various stages of trachoma.

tonometry based on the two investigations attention may be called to the fact that Leydhecker s series included a *greater number* of glaucoma patients with field loss at the primary *screening* In this connection it may be mentioned that among seven followed up patients *of the* present series who displayed a fairly extensive field loss at the *primary* screening further progression had developed in half of the eyes

Another question suggesting *itself is* whether it may be possible to clarify on the basis of the present investigation whether *patients* traced by routine tono metry but without glaucomatous field *loss* are particularly liable to develop field loss within a five *year observation* period compared with patients cha racterized as normal on routine tonometry

Various factors render a direct *comparison* difficult First only 32 per cent of the 1703 normals were subsequently *examined by* an ophthalmologist and no more than a scant half of *these were subjected to* tonometry Secondly as stated above only 68 of *the 110 patients* followed up had remained untreated *while in the remaining 42* patients the course was influenced by the instituted therapy

A follow up examination of normals disclosed no cases of glaucoma with *field loss* while both pressure values above the chosen screening level (20 mm *Hg) and rises to 25* mm *Hg* or higher (an arbitrarily chosen pathological level) *were recorded* Similar results were achieved by the author on previous follow *up* examinations of patients characterized as normal after tonometry among *patients admitted* to a medical unit (Nørskov 1967) and among members of the blood donor corps of Falster (Nørskov *1970a) This is also* in agreement with Linner & *Strömberg s* experience based on a five year follow up of 6a9 per sons born between 1896 and 1905 *who originally had* a tension value of 4 0/5 5 *or higher Further* Armaly (1969) who closely followed for up to ten years *a defined normal* group comprising *3936* persons could only in four cases dis close visual field defects to be characterized as glaucomatous on the basis of the chosen criteria

Compared with this none of the 68 untreated patients *included in the* pre sent study presented glaucoma with field loss while as in the normal group rises to pressure levels of 25 mm Hg or higher were recorded

If one chooses instead to base the comparison on the borderline cases – five treated and 43 untreated patients – singled out on the primary screening as a special risk group two patients were in fact found to have developed glaucoma with field loss Note however that in one of these two cases the discs had originally been characterized as glaucoma suspicious The case was however according to the chosen criteria referred to the group of borderline cases

That a group which is liable to develop visual field defects must be in cluded among the patients singled out by routine tonometry in ophthalmic prac tice is evident from the fact that despite treatment presence of or further de

Summary

141 cases of trachoma were studied with a view to find out if trachoma could give rise to increased ocular tension Scleral rigidity was also derived in these patients lest there might be a wrong tonometric conclusion 5 67 % of the eyes recorded a tension above 22 mm Hg while their scleral rigidity was normal statistically Hence the importance of thorough investigation of trachomatous cases especially late stages to exclude glaucoma has been stressed

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velopment of visual field defects were noticed in ten patients (14 eyes) Seven of these would however probably have been caught by ophthalmoscopy presence of central vein thrombosis or elucidation of a familial predisposition a circumstance which stresses the importance of these factors in glaucoma tracing On the other hand to judge from the results of the present investigation the water provocative test yielded no prognostic suggestions neither for patients displaying additional glaucomatous field loss during the observation period nor for patients with a rising pressure level to an arbitrarily chosen pathological value of 25 mm Hg or higher in the course of the observation period The same impression that the water provocative test has a very limited possibility of prognosticating the further course has been stated by Armaly (1969) and by the author on the basis of a previous follow up study (Norskov 1970a)

It would be well if the results of the present investigation might serve to suggest a modification of the screening procedure so as to reduce the number of patients suspected of glaucoma and at the same time facilitate encircling of patients being particularly liable to develop visual field defects In the present investigation similarly as at the primary screening it was chosen to study the consequences of altering the screening level to ≧ 21 mm Hg ≧ 22 mm Hg and ≧ 25 mm Hg respectively and to undertake a graduation according to age using a screening value of 22 mm Hg or higher for the age group of 35–64 and 25 mm Hg or higher for that over 65

Reservation must in any case be made with regard to reflections of this kind with a view to suggestions for altering the glaucoma screening procedure on the basis of a limited series of patients The problem to be considered is in fact that of the margin of security with which one desires to work within the field of glaucoma screening provided one attributes a central position to routine tonometry If we may be justified in drawing certain conclusions on this basis it seems that choice of 21 mm Hg as the screening level may be permissible This has in fact often been indicated as an appropriate screening level when applanation tonometry is employed (Goldmann 1960 Schmidt 1960 Becker & Shaffer 1965 Chandler 1965 Leopold 1967 Pollack 1967)

The results of the present investigation also suggest that a screening level of 22 mm Hg might be considered for patients ranging in age from 35 to 64 On the other hand the remaining suggestions for altering the screening level probably cannot be insisted on without definitely departing from the fundamental principles of routine tonometry

Another possibility of improving the screening procedure might be based on the fact that 60 per cent of the patients aged over 75 had died within a five year period A review of this group disclosed that all the patients presenting further development of glaucoma during the observation period also had had glaucomatous or glaucoma suspicious optic discs recorded on the primary screening However at the same time it was noticed that one of the three patients who

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From Carlanderska Sjukhemmet Gothenburg Sweden

AQUEOUS LEAKAGE THROUGH THE UVEAL VESSELS – A FACTOR IN CHOROIDAL DETACHMENT?

BY

BENGT ROSENGREN

The kind of choroidal detachment seen after operations for glaucoma and cataract was first studied systematically by *Fuchs* in 1900 and 1902 Its incidence after cataract operations was stated to be 4 7 per cent and that after iridectomy 10 per cent This condition – including ocular hypotension abolished anterior chamber and choroidal detachment – was attributed to postoperative lesions by *Fuchs* In some eyes examined histologically after cataract operations *Fuchs* observed rupture of the iris root at the point of attachment of the ciliary body to the sclera and he concluded that this enabled aqueous humor to be transported to the suprachoroidal region.

In 1912 *Meller* advanced a theory with other aspects In his opinion a post operatively persistent fistula to the exterior was a significant factor This would lead to leakage of aqueous humor and/or fluid from the vitreous and subsequent vitreous shrinkage *Meller* took into account the fact that choroidal detachment predominantly occur at high age levels something he attributed to the greater scleral rigidity exhibited in these age groups Together with this higher rigidity shrinkage of the vitreous would be responsible for the choroidal detachment

Hagen (1920) subscribed to the view of an external fistula as a significant factor This explanation was sufficient in those cases in which an external fistula was present which among other things appeared from the rapid disappearance of the symptoms – hypotension abolished anterior chamber and choroidal detachment – as soon as the fistula could be closed *Hagen* postulated that in those cases where no direct external fistula could be demonstrated an

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developed glaucomatous field loss despite normal conditions at the primary screening actually belonged to this age group

Nevertheless it is tempting to aim at modifying the glaucoma screening procedure by forbearing routine tonometry in the cases of patients aged over 75 because one should in any case be reserved with regard to administering miotics to patients of this age class unless glaucomatous field loss is present

If finally we consider the age at the time of routine tonometry of the patients with visual field defects at the follow up we see that nine out of 12 patients with simple glaucoma and field loss ranged in age between 59 and 71 This is the age group which Strömberg (1962) among others pointed out as the group most liable to development of an intra ocular pressure above 25 mm Hg This means that no matter which glaucoma prophylactic measures one prefers to go in for special attention should in addition be concentrated on the stated age group

Empolyment of routine tonometry will further as in the present study involve that a considerable number of patients from the group with ocular hypertension are singled out as glaucoma cases according to the current criteria and consequently treated In the present study it could not fail to impress one that several of the treated patients without glaucomatous field loss expressed complaints of a rather massive visual impairment A very thought provoking description of these therapeutic troubles has been given by a colleague under the name of "the miotic life (1964) A concurrent cause of these therapeutic complaints was doubtless the fact that in the endeavours to obtain an ideal normalisation below 20 mm Hg the group of patients concerned was an intensely treated one but that as stated normalisation was nevertheless obtained in a small number of cases only

Within recent years however the attitude held towards treatment of glaucoma without field loss seems to have altered While previously as expressed by Schmidt (1960) and others the view was adhered to that treatment ought to be instituted when the intra ocular pressure exceeded 22 mm Hg the pressure range of 25–30 mm Hg now seems to be preferred unless glaucomatous field loss is present (Chandler 1965 Shaffer 1967 Leopold 1967 1969 Snydecker 1969) Such an altered attitude must necessarily influence the placing of routine tonometry within the glaucoma prophylactic work

Conclusive remarks In evaluating the results achieved we must bear in mind that the observation period was five years only and that therapy had been instituted in some cases while on the other hand one fourth of the glaucoma suspects were recorded to have died within the observation period and an ideal normalisation to below 20 mm Hg had been obtained for a small proportion only of the treated patients despite intensive therapy

Our main impression of the investigation reported above must be that the very considerable number of patients with ocular hypertension who on routine

occult external microfistulation served as a similar causative factor *Hagen* stated that the incidence was 22 per cent after cataract operations and 76 per cent after Elliot trepanation

Hagen was able to demonstrate that the suprachoroidal fluid was neither aqueous humor nor vitreous humor but a fraction much richer in proteins probably a transudate from the choroidal induced by the low pressure This statement has later been confirmed by *O Brien* and by *Dobree* who using more modern techniques found an albumin value of 5 3 per cent

In a paper published 1961 *Chandler* & *Maumence* drew attention to the fact that choroidal detachment frequently occurs under conditions incompatible with the presence of an external fistula for example cases in which the condition be comes manifest a long time after the operative intervention They discussed, from this point of view whether afunction of the ciliary body s secretory activity might not result from primary low detachment of the ciliary body

Nevertheless the generally accepted view whenever no external fistulation can be demonstrated seems to be that some form of occult external microfistula tion is present However the following case which recently came my way seems to suggest another possible explanation

A female patient aged 73 with an advanced glaucoma in both eyes

V r 5/7 (+ 0 50) l 5/10 (± 0) T appl r 38 l 45

Visual fields r central rest 10° (Bjerrum 4/1000) l central rest 5° (Bjerrum 4/1000)

Despite maximal drug therapy for glaucoma the tension could not be normalized

Right eye

29/1 iridencleisis according to Stallard

12/2 normal healing conjunctival sutures removed

14/2 bleb at 12 o clock T = 10/5 5

18/2 low bleb at 12 o clock T = 10/55

3/3 V = 5/10 (+ 1 0) Barely manifest bleb T = 15/5 5

Choroidal detachment nasally at the margin

17/3 V 5/10 (+ 1 0) Shallow anterior chamber T = 13/5 5 High choroidal detachment

Attempts were ineffectively made with Pilocarpine × 3 and later Corotone × 3

25/5 It was noted in the records that the patient s vision 3 days previously was so re duced that she could not discern the windows Now the tension previously barely mea surable had risen to appl 32 and V = 5/10 Given Diamox After some days T drop ped to 0 and the choroidal detachment returned and became total

5/4 V = 0 T = 17/5 5 The choroidal detachment was total so it was decided to carry out

8/4 Psychrodiathermy over the iridencleisis region*

9/4 No definite improvement Chamber remained extremely shallow and T = 10/5 5

Tension measurements on subsequent days repeatedly showed that in about 5 seconds T dropped from 12/5 5 to 15/5 5 The conjunctiva had healed and the bandages after

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* Diathermy combined with cooling of the surface by means of ice cold distilled water dropped around the ball electrode

tonometry became suspected of glaucoma but otherwise presented normal conditions would have no great chance of developing glaucomatous field loss within a five year observation period Glaucomatous field loss was mainly found among the patients showing this defect at the primary screening among patients with central vein thrombosis and among patients with a familial predisposition Finally the present investigation also showed that patients with ocular hypertension at the follow up were recruited even from the group acquitted of glaucoma suspicion on routine tonometry

The suggestions advanced on the basis of this study with a view to modifying the screening procedure though with consistent employment of routine tonometry and at the same time obtaining a more effective encircling of the patients liable to develop glaucomatous field loss showed that any alteration whether great or small would add to the risk of missed glaucoma cases and consequently to a limitation of the glaucoma prophylactic value of routine tonometry

Finally to judge from the results of the present investigation it seems as if the most effective efforts against development of damages due *to glaucoma must still consist in transferring as much as possible of the work required to carry through routine tonometry on an intensification of control* and treatment of glaucoma with *field loss In addition it is important to concentrate particular attention on patients belonging to the age group of 60–70 this group being most liable to develop glaucomatous field loss*

Summary

In the present paper an account is given of the results of a follow up carried out five years after routine tonometry among 1882 patients aged over 35 seen in ophthalmic practice

The investigation comprised 169 patients with a pressure value of 20 mm Hg or higher 10 who also were suspected of glaucoma and finally 538 with pressure values below 20 mm Hg who re consulted the ophthalmologist within the observation period

Of the group of 169 patients 110 (65 per cent) were subjected to follow up examination 46 had died within the observation period and 13 could not be followed up for different reasons

The assessment of this group with *ocular* hypertension was based mainly on the 110 patients followed up The criteria chosen effected that 50 patients were characterized as suffering from glaucoma but only seven with fairly extensive field loss while 48 were characterized as borderline cases and 12 as *normal*

Of 68 untreated patients none developed glaucomatous field loss during the

diathermy – retained 3 days – exhibited no trace of moisture. It was believed that the fallin$_g$ tension revealed by the tension measurements could be explained only by in ternal leakage. Such an internal fistula had to be located in the small iridencleisis region and therefore 16/4 *a plastic plomb was applied over this region*

A radially situated silicone plomb was attached with sutures in the conjunctiva and anchored in the sclera with the plomb outside the conjunctiva (Fig 1) After applica ti n of these sutures it was noted that the tension dropped sharply so that the bulb seemed almost collapsed However the same evening the bulb had resumed its normal shape and the next morning the anterior chamber had normal depth T = 4 5/5.5

After 48 hours the choroidal detachment persisted only nasally and temporally After 3 days the choroidal detachment had disappeared after 5 days the plomb was removed 23.4 flushing at the site of the plomb Fluorescein test negative

14/5 V = 5/10 (± 0) Diffuse bleb at 12 o clock. Ophthalmoscopy and visual fields as before operation T appl = 10

In this case a variety of facts indicate that the operative intervation had not induced an external fistula Normal healing commenced and the conjunctival sutures were removed after 15 days The tension was 10/5 5 and a bleb was present over the iridencleisis region. A fortnight later however the bleb had disappeared and the tension dropped to 15/5 5 and simultaneously incipient choroidal detachment was noted Moreover after subsequent psychrodiathermy over the operative field the patient wore bandages for 3 days When these were changed no signs of moisture were observed

Assuming that no external fistula was present the rapid fall in tension ob served at tonometry according to Schiotz and the disappearance of the symp



Fig 1
The sil c ne plomb attached over the iridencleisis region

observation period In three of these the pressure level rose to 25 mm Hg or higher but otherwise no alteration in principle was observed towards a higher pressure level in this group

Among 42 treated patients only 18 per cent of the eyes had the pressure level reduced to below 20 mm Hg while 52 per cent had a pressure level of 22 mm Hg or higher Three patients who had previously been declared normal on the basis of ophthalmoscopy and visual field measurement developed glaucomatous field loss while in the remaining seven patients with progression during the observation period ophthalmoscopic changes presence of central vein thrombosis or a familial predisposition had been recorded on the original screening

Of the 538 patients with a screening value below 20 mm Hg who re consulted the ophthalmologist within the observation period 222 or 13 per cent of the original 1703 normals had their intra ocular pressure measured In four of these the measurement gave a value of 25 mm Hg or higher but without glaucomatous field loss being demonstrated

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toms after application of a silicone plomb suggest that escape of fluid via uveal vessels had taken place in this case At present nothing can be said as to how common this phenomenon might be

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FOUR FAMILIES WITH THE DOMINANT INFANTILE FORM OF OPTIC NERVE ATROPHY

BY

C C KOK van ALPHEN

History

In the last eight years there has been much more interest in hereditary optic nerve atrophy especially in the infantile forms

The *former confusion between the* Leber type and the dominant and recessive infantile forms now belongs to the past In the following survey of the literature of the last eight years we exclude publications about the Leber form of optic atrophy as well as publications about that group of *hereditary* optic atrophies which are associated with cerebral or other neurological disturbances (the Behr form etc)

François c s published in 1960 a comparitive study of acquired colour vision defects associated with the different types of hereditary optic atrophy In the Leber type he found red green defects in the dominant infantile form blue green defects

Marschall c s (1963) described a family with two sisters with the typical picture of the dominant infantile form of optic atrophy (D I O A) Two children of these sisters showed the typical form two were dubious cases with temporal pallor of the optic disc and quite good vision three children were unaffected

Ferdinando (1963) described a family with D I O A He did not mention colour defects in this family

Cernet (1963) published a family with D I O A combined with deafness

Grutzner (1963) described a pedigree with 55 cases In three of these the disease started between the second and third year Four cases showed functio

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Fig 5



Fig 6

structed section is more extensive but the patent part of the canaliculus ad joining the sac reaches to the lacrimal lacus an artificial lacrimal punctum is formed by a trephine above the tip of the inserted retrograd cannula (Fig 6) It should be mentioned here that the X ray contrast medium pumped through the intact canaliculus or if both canaliculi are obstructed percutaneously into the lacrimal sac hardly ever reaches up to the obstruction Therefore it is problematic to determine by X ray the exact site of the obstructed section of the canaliculus

In cases of obstructed canaliculi – of course – also we attempt probing too For better and more prolonged dilatation of the obstructed canaliculus Hyasone and own blood serum is added to the anaesthetic solution injected into the scarred area Then we fill up the canaliculus with cysteine solution to promote epithelisation Our results are encouraging but rarely lasting in more extensive obstructions

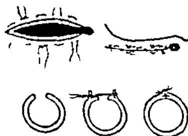


Fig 7

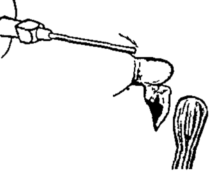


Fig 1

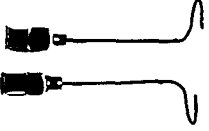


Fig 2

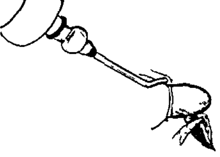


Fig 3

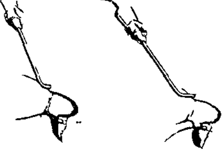


Fig 4

stump of the lacerated canaliculus too and the rupture is united in the usual manner

To employ the retrograd cannula seems preferable to the other retrograde procedures (5 6 7 8 9 10 11 12) as it is quite easily introduced following the simultaneous syringing and as the thread is driven within the canule the canalicular epithelium is not exposed to further damage

If the lacerated canaliculus can t be approached even from the intact one or if both canaliculi are lacerated or obstructed the retrograde procedure must be performed from the incised sac

The retrograde procedure enables us also to gauge the length of the ob structed part of the canaliculus The impassable part can be flanked by the retrograd cannula from the sac and by a Bowman s probe from the lacrimal punctum (Fig 5) A few mm s of the canaliculus may then well be excised and the two stumps – round a plastic thread – united perfect end to end If the ob

nal defects but no ophthalmological abnormalities He found bluecolour defects and in some cases abnormal dark adaptation

Klein (1964) discussed a symposium on hereditary optic atrophies

Rivara (1964) examined by static perimetry the fields of vision in three cases in a family with D I O A who had a fairly good visual acuity (0 4 0 5) He found enlargement of the blind spots and a limitation of the peripheral fields

Rose (1964) gave a useful description of the various ways in which optic atrophy can be classified

Schwartz (1964) described 48 children with optic atrophy without evidence of diffuse cerebral or systemic disease but no information about the heredity is given

Bergamini (1964) mentioned a family with congenital optic atrophy with ptosis aniridia, cataract and nystagmus

Proto (1965) published a family with D I O A in which especially women were affected

Kozousek (1965) reported a dominant hereditary optic nerve atrophy approaching Kjer s form with asymmetry of the face dental anomalies deformation of the ears and the tongue and lowered intelligence

François (1966) published a very informative paper Congenital or infantile optic atrophy of autosomal recessive heredity is rare

Jaeger & Grützner (1966) described the changes in the colour sense in familial macular degeneration and in hereditary optic atrophies Patients with macular diseases show anomalies in colour sense for red green patients with D I O A anomalous blue vision

Grützner (1966) examined members of four pedigrees with D I O A for haptoglobin components of the serum and also for the various blood groups There was no indication that there was a genetic linkage between these haematological conditions and the ocular manifestations In addition there was no evidence to suggest a linkage between this inherited form of optic atrophy and the inherited low voltage E E G which was found incidentally

Jaeger (1966) emphasizes that the differential diagnosis of the hereditary optic atrophies in childhood is of great importance with regard to prognosis Patients with D I O A can mostly be trained in a normal school and later on can support their families but patients with the congenital dominant or recessive form must follow an occupation for the blind or at the best for the partially sighted

Hellner & Haase (1967) performed electro retinographic studies in two families with D I O A Disorders of the photopic E R G were observed Lower photopic potentials and reduced maximal flicker fusion frequencies were characteristic

The increment threshold determined electroretinographically in increasing light adaptation demonstrates a lowered general sensivity of the retina compared with a normal control group

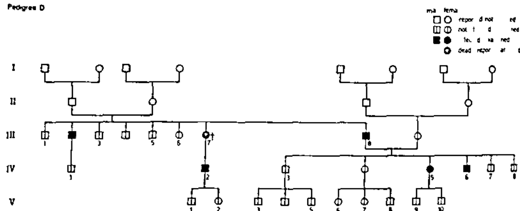


Fig 4
Pedigree D

Discussion

Time of onset of the disease

In all four pedigrees the time of onset was in the early years of childhood generally between 3 and 10 years of age the youngest affected child known was 1 year old

In our material the disease has not yet been demonstrated at birth which fact seems to exclude the congenital form A few cases of nystagmus were however noted in pedigree A

Abnormalities of the fundus

Optic nerve atrophy was found in all four pedigrees In pedigree A B and D no dubious cases existed On the other hand pedigree C showed cases with normal fundi and poor vision and vice versa In pedigree D the papillae were totally white with no difference between the temporal and nasal sides

Visual acuity

In the serious cases of pedigree A B and D vision was less than 0 1 in the slighter cases 0 2 0 5

In pedigree C no serious cases were found

Refraction

In all affected members of the four pedigrees myopia was found

Rorsman (1967) and *Rose* (1966) describe optic atrophy combined with diabetes mellitus in children of 14 18 years of age

Smolin (1967) reported one family with D I O A

Wilson (1967) reports in a paper on several forms of optic atrophy Patients with D I O A in whom the disease occurs at an earlier age have a worse visual prognosis

Michal (1968) emphasizes again the three forms of hereditary optic atrophy e g the D I O A the congenital or infantile recessive form and the Leber type

Present Investigation

Our own investigation concerns four Dutch pedigrees with D I O A Thanks to the Netherlands General Association for Prevention of Blindness fieldworkers of this Association did much work in determining the family relationships and in investigating many members of the families scattered throughout the Netherlands

Pedigree A

The first pedigree about which I published a paper in 1960 was totally reinvestigated in 1967 1968 The affected members did not seem worse than in 1960 The younger affected children of family VI 8 20 showed a slight increase in myopia. Visual acuity with correction however did not diminish There were still no signs of optic atrophy in the body VI 19 who seemed unaffected in 1960 However one more girl (VI 20) had been born in this family and I could follow this child closely myself At the age of two years though a distinctive pallor of the temporal part of the disk was seen the girl seemed to have a normal visual acuity for her age Now at the age of six the vision is OD 0 2 OS 0 3 and she shows clearly a red green colour defect She shows no strabismus as yet Probably the disease was not congenital I have seen this child many times since birth The colour vision of this large family was tested again with the H R R test but no blue yellow defects were noted The family VI (8 20) living in Leyden could be examined by myself at will The affected children showed red green defects at the age of 4 6 years as soon as they could be examined for colour vision

As I noted in my previous paper the expression of the diseases in this family is very variable The younger generation is definitely less seriously affected than the earlier ones However the identical twins (VI 48 and 49) are socially blind and have had to attend a school for the blind Nystagmus was only noted

Strabismus

In pedigree A and B we found strabismus divergens in all affected members In pedigree C and D no strabismus has been seen

Visual fields

Wedge formed peripheral defects already described in 1960 were found in some members of pedigree A

The affected members of pedigrees B C and D had in general no peripheral defects only III 38 showed slight concentric limitation All affected members of the four pedigrees showed enlargement of the blind spot and/or paracentral scotomata

Colour sense

Pedigree A was again investigated with the H R R. test The serious cases had achromatopsia the slighter cases distinct red green defects In pedigree B also we found achromatopsia in the serious cases in the slight cases some red green defects definitely no blue defect. On the contrary some members of pedigree C showed slight blue defects Some cases in pedigree D showed red green as well as blue yellow defects When comparing these pedigrees with other extensively investigated pedigrees (Jaeger Grutzner Kjer etc) it is notable that pedigrees A and B definitely show no typical disturbance of blue yellow perception on the other hand pedigree B shows a definite defect in red green colour vision Pedigree C shows a slight disturbance in the blue in a few cases colour vision being more often normal in the affected sibs of this family

Pedigree D is exceptional in having both colour vision defects

A comparison of the above mentioned symptoms in the four pedigrees is made in table I

Nystagmus

This symptom was only observed in pedigree A in three of the most serious cases (V 4 V 13 V 15)

Electroretinography

Except in some very serious cases no abnormalities were found in pedigrees A B and C No E R.G s are available from pedigree D

No other physical or neurological anomalies were found

Heredity

The pedigrees A and B are in agreement with the rules for dominant autosomal

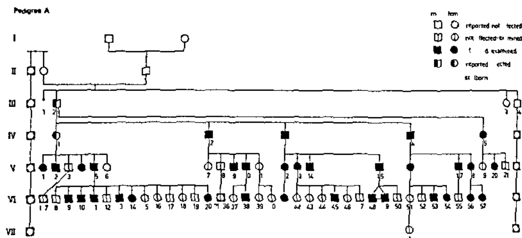


Fig 1
Pedigree A

in three cases (V 4 V 13 V 15) No new cases were found with the exception of VI 20 The two eldest affected sons of the Leyden family (V I9 and VI 10) are engaged to be married and it will be interesting to see the development of their children later on However some members of the family have purposely adopted children so we will not be able to follow the affection in their off spring

Pedigree B

The members of this pedigree were for the most part examined at the Eye Hospital in Rotterdam all the families live in the neighboorhood of this town Much work was done on this pedigree of which only a small part proved to be affected The members who show the disease resemble closely the affected members of pedigree A

The older generation is more seriously affected than the younger wone with visual acuity less than 0 1 some of them show strabismus divergens (VI 87 and 89) In generation V again myopia occurs The girl V 134 was quite normal up to her 12th year then her visual acuity deteriorated to 0 5 the disks showing an increasing temporal pallor A follow up of the fundus by colour photo graphy was made The F R G was normal the Bjerrum showed somewhat en larged blind spots

The boys V 142 and V 143 were affected at a somewhat younger age V 142 had obvious signs of pallor of the disks and visual acuity ODS 0 3 at the age of 10 years V 143 had visual acuity ODS 0 3 at the age of 7 years

They both deteriorated to a vision of ODS 5/60 0 1 and although they had

Table 1

	Vsion		Rf cto d		
	S o s ca s	L ght ca s	St b m s	V s al f elds	Colou
Ped g ee A	< 0 1	0 2 0 5	myop a d e ge t t b s m	wedge haped defects p ce t al scotom t	d fect ed g ee
P d g ee B	< 0 1	0 2 0 5	my p d e g f st ab mus	pa cent al ot mat	bl e d f cts
P d g ee C	no se ou s	0 2 1 d b s ca s	my p no t ab smus	pa central scotomata	d b o s bl e d fects
Ped g D	< 0 1	0 25	myop a o st ab mus	p ace t l otom t	d f cts n ed g + bl e yellow

heredity Both pedigrees show affected members in more than two generations The ratio of affected to healthy individuals (theoretically 1 1) is in pedigree A for the 14 sibships of the generations IV V and VI – all offspring of affected parents – 34 24 in pedigree B for the four sibships of the generations IV and V 7 8

The pedigrees C and D differ from A and B in that they as yet only show affected members in two generations and in that in the first affected generation three diseased sibs have appeared This could suggest recessivety but the fact that in both pedigrees the off spring of the affected parent include several affected children is more suggestive of dominance In the pedigrees A B and D X chromosomal heredity can be excluded by heredity from father to son The fact that in pedigree C women and men are equally affected also argues X chromosomal heredity

In pedigree A in particular the expression is very variable

In none of the pedigrees does the disease skin a generation

The mutation can probably be found in

Pedigree A III 2

Pedigree B III 28

Pedigree C } unknown because in the first affected generation three members
Pedigree D } show the disease

Summary

Two pedigrees with a dominant infantile form of optic atrophy and two pedigrees with a probably dominant infantile form of optic atrophy are described

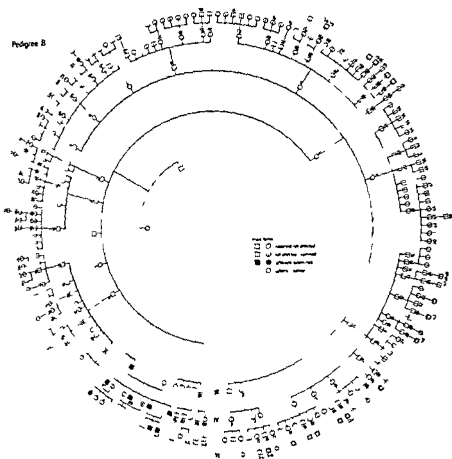


Fig 2
Pedigree B

normal peripheral fields of vision they had to be trained in a school for the blind

As to the colour vision blue green defects were definitely not observed In the serious cases it was not possible to do colour investigations In the other members no colour defects or only very slight green red defects were found E.R.G s and dark adaptation curves were normal the latter in the more serious cases somewhat too high

A very interesting fact is that patient IV 89 who is seriously affected married by second marriage a woman known to have Leber s optic atrophy She figures in a pedigree of Waardenburg and in one of van Senus Out of this

The disease develops during childhood The expression of the disease is variable vision 0 0 2 0 5

The abnormalities in the fundus are very typical pale disks most often whiter on the temporal side

In most cases the visual fields are peripherally normal In some cases in pedigree A wedge formed peripheral defects were found and in one case in pedigree C a slight concentric limitation In all affected cases there are enlarged blind spots or paracentral scotomata

In the serious cases achromatopsia is found The slighter cases in pedigrees A and B show a definite disturbance in red green vision In pedigree C how ever some sibs show defects in the blue Pedigree IV shows blue yellow as well as red green defects Electroretinography gives fairly normal results

Because of the good peripheral fields of vision all the less seriously affected individuals can maintain themselves in the community

As far as we can determine the disease is not congenital It is however of importance to examine the new born children as early as possible When mak ing a differential diagnosis in a case of optic nerve atrophy the general oph thalmologist must be aware of the existence of this affection

Several neurosurgical operations and needless neurological investigations could have been spared if some time had been given to a simple investigation of the patient s family

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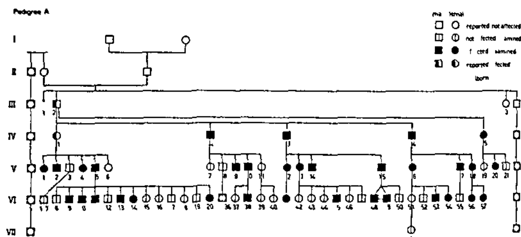


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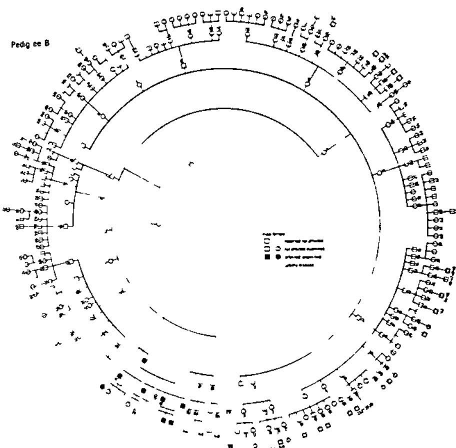


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Aus der Universitäts Augenklinik Jena
(Direktor Prof Dr med habil A Heydenreich)

NYKTOMETERUNTERSUCHUNGEN BEI MAKULAERKRANKUNGEN

VON

JOHANNA ORTLEPP

Einleitung

Hin und wieder stehen wir bei unserer augenärztlichen Untersuchung einer Diskrepanz zwischen den Klagen des Patienten über sein schlechtes Sehvermögen und den sehr guten subjektiven Visusangaben bei der Prüfung an unseren Sehprobentafeln gegenüber Die Ursache ist in Folgendem zu suchen

Wir berücksichtigen bei der üblichen Sehschärfeprüfung nicht die Zeit die zur Erkennung eines Sehzeichens benötigt wird Die Sehschärfeprüfung findet bei günstiger Beleuchtung statt Sehzeichen und Grund weisen einen starken kontrast auf Bei den vielfältigen täglichen Anforderungen aber die an die Sinnesleistung des Auges unseres Patienten gestellt werden spürt der Patient sein Unvermögen denn hier liegen oft nicht so günstige Leuchtdichtebedingungen vor wie bei unserer Visus Prüfung

Wir haben bei Patienten mit guter Sehschärfe aber feinen makulären Veränderungen am Registrier Nyktometer des VEB Carl Zeiss Jena das auf das Nyktometer von COMBERG zurückgeht Sofortadaptation und Blendempfindlichkeit untersucht mit der Fragestellung

Liegen die Prüfungsergebnisse im Normbereich wie er für die verschiedenen Altersgruppen gefunden wurde?

Gibt uns das Registrier Nyktometer eine bessere Information über die Funktion bei Makulaerkrankungen als die übliche Visusprüfung?

Eingegangen am 5 December 1969

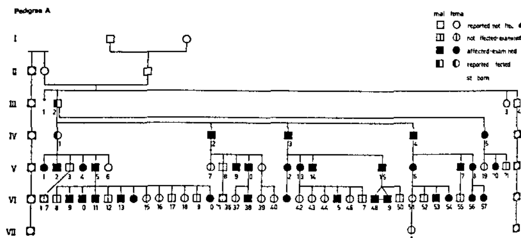


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them were unable to see any of the H R R plates Generation IV had two affected and six dubious cases As to the dubious cases

IV 23 has normal vision temporal pallor of the disks and only 5 capillaries

IV 35 has normal visual acuity (Vis ODS with s – 2 =) but a definite pallor of both papillae

IV 34 has poor vision (Vis ODS with s – 1 = 0 25) but no visible pallor of the papillae.

IV 36 has slight pallor of both disks and a visual acuity of ODS 0 3

IV 38 has normal vision slight temporal pallor of the papillae and some concentric narrowing of the peripheral fields of vision

IV 39 is like IV 23 Vis ODS 1 temporal pallor of the disks 6 small vessels counted

Visual fields were generally normal peripherally (except IV 38) The definitely affected members showed paracentral scotomata

Some of the less affected and dubious cases showed a dubious blue defect definitely no red green defect the more serious cases could not name any colour

A further investigation into the colour vision of this pedigree is still going on at the Utrecht Hospital and will be published later

One patient (III 11) underwent many needless examinations by neurologists and other pecialists because no diagnosis of her condition could be made Needless to say how much time and trouble could have been spared by a better anamnestic investigation of the family

Pedigree D

Because the members of this pedigree are living to the North of Amsterdam they were investigated at the University Eye Clinic of that town

The fundi resemble those of the affected members of the first three pedigrees They all show pale papillae but in the members of this pedigree all disks are totally white

The periphery of the visual field is normal but the blind spots are enlarged The affected members of this pedigree have defects of colour vision both red green and blue yellow

Case IV 6 shows defects of red green as well as yellow blue vision.

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In the most serious cases investigation of the colour vision was impossible (III 2 and 8 IV 2)

Case III ı was deceased at the time of the investigation but reported affected

ration wurden + 4 0 und +5 0 D spharisch gebraucht auch bei Retinitis zentralis serosa einmal + 4 0 D spharisch

Die Untersuchung erfolgte monokular einmalig bei nicht erweiterter Pupille. Eine weitere Untersuchung mit Minusglasern diente zum Ausschluss einer Nachtmyopie In den vorliegenden Fallen konnte keine solche nachgewiesen werden

Bei den Verlaufsuntersuchungen der *Retinitis zentralis serosa* war bei einigen wenigen Untersuchungen die Pupille erweitert In diesen Fallen wurde die *Helladaptation am Gerat stenopaisch vorgenommen um eine nachhaltige Blendung zu verhindern* Der Vergleich mit den zuvor und danach bei enger Pu*pille erhaltenen Ergebnisse gestattete uns* die so gewonnenen Untersuchungsergebnisse mit in die Tabelle aufzunehmen Der Patient wurde zu schnellen Angaben am Nyktometer angespornt Eine Zeile galt als richtig gelesen, wenn von den 5 angebotenen Zahlen 4 richtig erkannt wurden

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Ergebnisse

Sofortadaptation

Von unseren 46 gepruften Augen erreichten 19 am Nyktometer keine Sehscharfe die Sofortadaptation war vollig aufgehoben (Tab 2) 9 dieser Augen hatten eine Sehscharfe von 5/4 an der Sehprobentafel 12 erlangten einen Visus von 0 1 und 11 einen von 0 2 im Verlauf der Sofortadaptation (Tab 2)

Diese Werte liegen bei Berucksichtigung des Alters das bei der Beurteilung der Sofortadaptation und Blendempfindlichkeit nach Braun Heinsius Schober Aulhorn und Harms Sachs Lehnert und Schmidt wesentlich ist nicht mehr innerhalb des normalen Streubereiches *

4 Augen liegen mit einem Visus von 0 3 am Nyktometer noch im unteren

---

* Fur die Aufstellung der Alters bhangigen *Normalwerte am Registrier Nyktometer* des VEB Carl Zeiss Jena danke ich Fraulein cand med G Geyer

marriage one daughter was born who is – up to now – quite normal The two daughters from the first marriage of IV 89 are normal too (V 138 and 139)

The investigation of heredity in cases of optic atrophy is of great importance This is for instance proved by the fact that member IV 91 was diagnosed as a case of Leber s optic atrophy and as such was operated upon by a neuro surgeon Of course this still rather dangerous operation has been without success The same fate overcame one of the members of pedigree A patient V 20 She too was operated on as a case of Leber s optic atrophy by another neuro surgeon in another town

If hereditary investigation had been done earlier these two patients would have been spared a useless operation

Pedigree C

As the members of this pedigree are living in the eastern provinces and in the new Zuiderzee diked provinces they were investigated as the Ooglijders Gasthuis in Utrecht

This pedigree differs from the first two It shows in addition to evidently affected members dubious cases as in the family described by Marschall In the third generation the patients 7 10 and 11 have the fully developed disease although their visual acuity is fair (0 2 0 5) Their fundi show temporal pallor of the disc An investigation counting the small capillaries on the papilla was made in this family Instead of the 8 9 capillaries seen on the normal papilla only 3 5 were found in these three patients It is remarkable that all three of

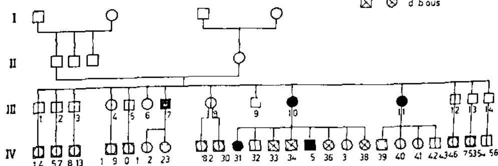


Fig
Pedigree C

Weiterhin wurden einige Patienten mit Retinitis zentralis serosa wiederholt während ihrer Erkrankung am Registrier-Nyktometer geprüft, um festzustellen wie sich Sofortadaptation und Blendempfindlichkeit während des Krankheitsverlaufes verhalten

Methodik

46 Augen an 36 Patienten der Universitats Augenklinik Jena wurden am Registrier Nyktometer des VEB Carl Zeiss Jena untersucht Davon wurden in 4 Fallen von Retinitis zentralis serosa mehrmalige Untersuchungen in einem Fall bis zu 14 während der Erkrankung vorgenommen In den übrigen Fallen handelte es sich um verschiedene Erkrankungen (s Tab 1) Abgesehen von den Makuladegenerationen und der Retinitis zentralis serosa galten die makularen Veranderungen aufgrund des ophthalmoskopischen Befundes als nicht mehr frisch sondern wurden als vernarbt angesehen

Altersmassig war unsere Patientengruppe ganz heterogen zusammengesetzt Die jungsten Patienten waren 15 die altesten 56 Jahre alt Nur 4 Patienten waren uber 50 Jahre alt 19 Patienten waren junger als 40 Jahre

Die brechenden Medien waren in allen Fällen klar

An der Sehprobentafel betrug die Sehscharfe 5/4 5/5 5/7 Die Nyktometerprufung wurde mit Fernkorrektur durchgefuhrt Die Refraktionen lagen im Bereich von + 2 5 bis – 2 0 D spharisch Jedoch in einem Fall von Makuladegene

Tabel 1
Makulaerkrankungen

Erkrankung der untersuchten Augen	Anzahl d Augen
Retinitis zentralis serosa	10
Chorioretinitis parazentralis	6
Chorioretinitis disseminata	10
Iridocyclitis mit Makulaveranderungen	5
Periphlebitis mit Makulaveranderungen	2
Chorioretinitis juxtapapillaris	1
Makuladegeneration	12
	insges 46

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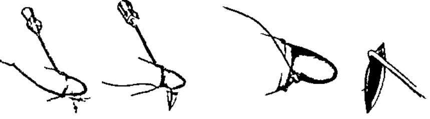
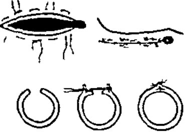


Fig 5 *Fig 6*

structed section is more extensive but the patent part of the canaliculus adjoining the sac reaches to the lacrimal lacus an artificial lacrimal punctum is formed by a trephine above the tip of the inserted retrograd cannula (Fig 6) It should be mentioned here that the X ray contrast medium pumped through the intact canaliculus or if both canaliculi are obstructed percutaneously into the lacrimal sac hardly ever reaches up to the obstruction Therefore it is problematic to determine by X ray the exact site of the obstructed section of the canaliculus

In cases of obstructed canaliculi – of course – also we attempt probing too For better and more prolonged dilatation of the obstructed canaliculus Hyasone and own blood serum is added to the anaesthetic solution injected into the scarred area Then we fill up the canaliculus with cysteine solution to promote epithelisation Our results are encouraging but rarely lasting in more extensive obstructions



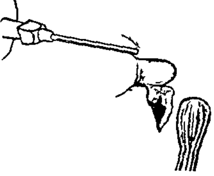


Fig 1

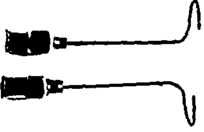


Fig 2

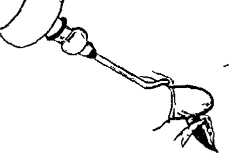


Fig 3



Fig 4

stump of the lacerated canaliculus too and the rupture is united in the usual manner

To employ the retrograd cannula seems preferable to the other retrograde procedures (5 6 7 8 9 10 11 12) as it is quite easily introduced following the simultaneous syringing and as the thread is driven within the canule the canalicular epithelium is not exposed to further damage

If the lacerated canaliculus can t be approached even from the intact one or if both canaliculi are lacerated or obstructed the retrograde procedure must be performed from the incised sac

The retrograde procedure enables us also to gauge the length of the ob structed part of the canaliculus The impassable part can be flanked by the retrograd cannula from the sac and by a Bowman s probe from the lacrimal punctum (Fig 5) A few mm s of the canaliculus may then well be excised and the two stumps – round a plastic thread – united perfect end to end If the ob

Weiterhin wurden einige Patienten mit Retinitis zentralis serosa wiederholt während ihrer Erkrankung am Registrier Nyktometer gepruft um festzustellen wie sich Sofortadaptation und Blendempfindlichkeit wahrend des Krankheits verlaufes verhalten

Methodik

46 Augen an 36 Patienten der Universitäts Augenklinik Jena wurden am Registrier Nyktometer des VEB Carl Zeiss Jena untersucht Davon wurden in 4 Fällen von Retinitis zentralis serosa mehrmalige Untersuchungen in einem Fall bis zu 14 wahrend der Erkrankung vorgenommen In den ubrigen Fallen handelte es sich um verschiedene Erkrankungen (s Tab 1) Abgesehen von den Makuladegenerationen und der Retinitis zentralis serosa galten die makularen Veranderungen aufgrund des ophthalmoskopischen Befundes als nicht mehr frisch sondern wurden als vernarbt angesehen

Altersmassig war unsere Patientengruppe ganz heterogen zusammengesetzt Die jungsten Patienten waren 15 die ältesten 56 Jahre alt Nur 4 Patienten waren uber 50 Jahre alt 19 Patienten waren jünger als 40 Jahre

Die brechenden Medien waren in allen Fallen klar

An der Sehprobentafel betrug die Sehscharfe 5/4 5/5 5/7 Die Nyktometer prüfung wurde mit Fernkorrektur durchgefuhrt Die Refraktionen lagen im Be reich von + 2 5 bis – 2 0 D spharisch Jedoch in einem Fall von Makuladegene

Tabel 1
Makulaerkrankungen

Erkrankung der untersuchten Augen	Anzahl d Augen
Retinitis zentralis serosa	10
Chorioretinitis parazentralis	6
Chorioretinitis disseminata	10
Iridocyclitis mit Makulaveranderungen	5
Periphlebitis mit Makulaveranderungen	2
Chorioretinitis juxtapapillaris	1
Makuladegeneration	12
	insges 46

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Tabel 4
Adaptationsdauer bei 0 2 Visus am Nyktometer

Adaptationsdauer in sec	Anzahl der Augen
41– 60	1
61– 80	3
81–100	4
101–120	3

bis zu einer Adaptationsdauer von 60 Sekunden Nach Tabelle 4 haben dann alle 11 Augen (das 1 Auge der Spalte 41 60 sec gehort einer 22jahriger Patientin) die die Sehscharfe 0 2 erreichen keine normale Adaptationsdauer

Von unseren 46 am Registrier Nyktometer des VEB Carl Zeiss Jena geprüften Augen mit makularen Veranderungen und noch guter Sehscharfe beim Tagessehen zeigten 42 eine Storung der Sofortadaptation die sich in 23 Fallen *in herabgesetzter Sehscharfe* in 19 Fallen sogar in volligem Verlust der Sofort*adaptation ausserte* Bei 21 Augen von den insgesamt 23 mit herabgesetzter Seh*scharfe liess sich* daneben eine Verlangerung der Adaptationsdauer nachweisen

Blendempfindlichkeit

Die Sehscharfewerte bei Blendung *sind in Tabelle 5 verzeichnet Bei der Be*leuchtungsstufe 8 erreichten 34 Augen von *insgesamt 46 keine normale Seh*scharfe, hatten also eine erhohte Blendempfindlichkeit *Bei der Beleuchtungs*stufe 64 waren 24 Augen noch erhoht blendempfindlich *Dabei waren unter den* Augen die bei Beleuchtungsstufe 8 erhohte Blendempfindlichkeit zeigten die 19 Augen wieder anzutreffen bei denen die Sofortadaptation vollig aufgehoben war 12 von ihnen fanden sich auch wieder unter den erhoht Blendempfindlichen bei Beleuchtungsstufe 64

Sofortadaptation und Blendempfindlichkeit im Verlauf von Retinitis zentralis serosa

4 Patienten mit Retinitis zentralis *serosa* konnten wir wahrend des Krankheitsverlaufes wiederholt am Registrier *Nyktometer des* VEB Carl Zeiss Jena untersuchen einen davon allerdings erst nach 5 *wochiger Behandlung*

Die Sofortadaptation ist wahrend der Erkrankung *in allen Fallen erheblich* herabgesetzt Wahrend die Sehscharfe beim Tagessehen mit *Plusglasern so kor*rigiert werden kann dass normale Werte erreicht werden ist das bei herab

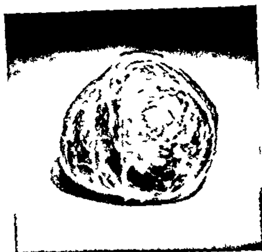


Fig 3
Large hemangioma Anterior wall presents a facet that molds the posterior wall of the eyeglobe



Fig 4
Section of hemangioma Hematoxilin Eosin – X 42 Large endothelium lined blood containing spaces indicating a cavernous hemangioma

Tabel 2
Sofortadaptation bei Makulaveranderungen.

Visus am Nyktometer	Anzahl der Augen	davon Visus an der Sehprobentafel		
		5/4	5/5	5/7
0	19	9	5	5
0 1	12	6	3	3
0 2	11	6	2	3
0 3	4	2	2	–

normalen Streubereich wie er von uns gefunden wurde und auch von Lehnert und Schmidt angegeben wird Es handelt sich dabei 2 × um eine Chorioretinitis parazentralis 1 × um eine Chorioretinitis disseminata und 1 × um eine Retinitis zentralis serosa

In Tabelle 3 und 4 sind die Zeiten angeben die für die erreichte Sehschärfe am Nyktometer benotigt wurden Normale im Alter von 40 49 Jahren brauchen bei monokularer Prufung fur die Erlangung der Sehschärfe 0 1 im Durchschnitt 22 Sekunden bei Berücksichtigung der Streuung bis 40 Sekunden Auch die Altersgruppe 50 bis 59 Jahre der einer unserer Patienten mit Visus 0 1 angehort beansprucht normalerweise keine langere Zeit Demzufolge erreichen nur 2 (der Patient ist 42 Jahre alt) von 12 Augen (s Tab 3) den Visus von 0 1 in einer normalen Zeit Bei den ubrigen 10 Fällen ist die Adaptationsdauer verlangert d h der Anstieg der Sofortadaptationskurve ist flacher als normal Die benotigte Zeit fur die Sehscharfe 0 2 streut bei monokular gepruften 20 29 jahriger bis zu einer Adaptationsdauer von 40 Sekunden bei den alteren Altersgruppen

Tabel 3
Adaptationsdauer bei 0 1 Visus am Nyktometer

Adaptationsdauer in sec	Anz hl der Augen
31– 40	2
41– 60	3
61– 80	2
81–100	3
101–120	2



Fig 1

Left exophthalmos Left eye is pushed straight forward

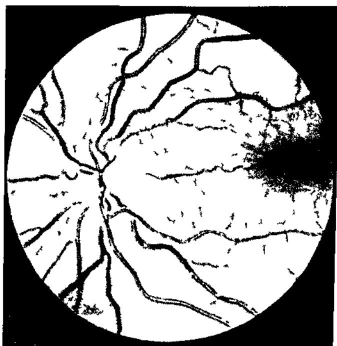


Fig 2

Posterior pole of the left eye showing retinal striae from disc to macular area

present Roentgen examinations of the skull and the orbits proved negative An angiography of the orbit demonstrated an abnormal displacement of the left ophthalmic vein

A Kronlein orbitomy was performed to explore the lateral and retrobulbar regions of the orbit When the index finger was introduced behind the eyeglobe an encapsulated tumor was easily separated from the surrounding tissues and removed The red firm tumor measured 30 × 21 mm and presented a facet in its anterior part which molded the posterior portion of the eyeglobe (fig 3) Histologically it consisted of endothelium lined blood containing spaces characteristic of a cavernous hemangioma (fig 4)

gesetzter Beleuchtung wie sie am Nyktometer herrscht nicht der Fall Auch bei einem Patienten der während des gesamten Verlaufes der Erkrankung auch ohne Korrektur uber volle Sehschärfe bei Tagessehen verfugt und lediglich eine Storung des qualitativen Sehens (Metamorphopsie am Amsler Netz) auf weist ist die Sofortadaptation erheblich herabgesetzt In Tab 6 sind die Un tersuchungsbefunde eines Patienten zusammengestellt. Mit der ophthalmosko pisch nachzuweisenden Abheilung des Prozesses in Makulabereich erholte sich in unseren Fallen die Funktion der Sofortadaptation soweit dass sie als normal zu bezeichnen ist Bis zu dieser Erholung verging bei 2 Patienten ein Viertel jahr

In Abb 1 haben wir einige Kurven der Sofortadaptation wie auch die ent sprechende Blendempfindlichkeit die zu verschiedenen Zeiten der Erkrankung eines Patienten aufgenommen wurden und das Wiedergewinnen der Funktion wahrend des Verlaufes der Retinitis zentralis serosa erkennen lassen darge *stellt Ein Übungseffekt wie er bei Normalen beobachtet wird* (Lehnert und Schmidt Patz) konnte wahrend der herabgesetzten Funktion der Sofortadap tation nicht nachgewiesen werden

Bei allen 4 Patineten ist wahrend der Erkrankung auch die Blendempfind lichkeit bei Beleuchtungsstufe 8 und 64 (Tab 6 Abb 1) erheblich in Mitleiden schaft gezogen Aber auch sie kehrt mit Abheilung der Erkrankung in den Normbereich zuruck

Diskussion

Aus den Ergebnissen der vorliegenden Arbeit geht hervor dass Sofortadapta tion und Blendempfindlichkeit am Registrier Nyktometer des VEB Carl Zeiss Jena bei makularen Erkrankungen dann schon start verandert sind wenn die Sehscharfe noch nicht betrachtlich herabgesetzt ist. Unsere Befunde bestatigen die Angaben der Literatur So berichten Venturi und Volpi uber starke Herab setzung der Sehscharfe bei herabgesetzter Beleuchtung bei Patienten mit maku laren Erkrankungen und uber eine leicht verzogerte Dunkeladaptation was vor allem im ersten Abschnitt der Kurve deutlich nachzuweisen war gepruft am Goldmann Weekers Adaptometer Auch Faraldi konnte bei differenzierter Pru fung des Lichtsinns am Goldmann Weekers Adaptometer bei Patienten mit er worbenen makularen Veranderungen Abweichungen von der Norm festzustel len Mazzantini und Tola fanden bei 38 Patienten mit morphologischen Maku laveranderungen aber normalem Visus in 30 Fallen eine deutliche Herabsetz ung des Visus mesopicus

Die Blendempfindlichkeit gepruft als Sehscharfe wahrend Blendung am Re gistrier Nyktometer war bei einem betrachtlichen Teil unserer Patienten er

The susceptibility of hemangiomas of the orbit to hormonal change the preg nancy in particular is emphasized

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Tabel 5

Sehscharfe bei Blendung

Die fettgedruckten Werte liegen innerhalb der Streubreiten Normaler 10–59 jahriger bei monokularer Prufung

Beleuchtungsstufe	Anzahl der Augen mit Visus										
	0 0	0 1	0 2	0 3	0 4	0 5	0 6	0 7	0 8	0 9	1 0
1	43	2	1	–	–	–	–	–	–	–	–
8	17	7	10	7	3	2	–	–	–	–	–
64	–	1	6	10	7	4	8	7	2	1	–

The postoperative course was uneventful The exophthalmos disappeared (fig 5) and two months after surgery the fundus presented normal features the visual acuity improved to 6/6 and the visual field presented a normal configuration

Discussion

The presence of an exophthalmos changing in size has been observed in orbital hemangiomata and usually linked to local bleeding It is of interest however to note that vascular tumors can grow under the influence of endocrine factors and pregnancy in particular Watson & McCarthy surveyed 1001 hemangiomas located at different sites of the body and pointed out that they occured more often in females (65 %) and are prone to start or increase rapidly in size with the onset of menses or at the beginning of pregnancy In the eye Reese observed in one patient the aggravation of a choroideal racemous hemangioma at the time of two pregnancies (3) and in another case the sudden growth of an orbital racemous hemangioma also during pregnancy (4)

In the patient reported in the present article the onset of exophthalmos during puberty and its growth during pregnancy is additional evidence that such orbital tumours are susceptible to hormonal changes The importance of these events in the differential diagnosis of orbital tumours is evident

Summary

A 31 year old pregnant woman presented with a growing unilateral exophthalmos which had been first noted during puberty Surgical exploration revealed an orbital cavernous hemangioma



Fig 5
Post operative appearance

?1 3	0 1 (0 7)	50	0 0 (0 2)	0 4 (0 8)	0 6 (1 0)	5/10 +1 5 = 5/4p	+	Makulareflex unregelmässig Präzipitate d Retina
1 4	0 1 (0 7)	68	0 0 (0 1)	0 4 (0 9)	0 8 (1 0)	5/5p +0 5 = 5/4p	+	Makulareflex unregelmässig Präzipitate d Retina
+10 4	0 2 (0 7)	108	0 0 (0 ?)	0 2 (0 9)	0 55 (1 0)	5/4p Gl b n	+	Makulareflex unregelmässig Präzipitate d Retina
17 4	0 2 (0 7)	77	0 0 (0 2)	0 4 (0 8)	0 9 (1 0)	5/4p Gl b n	+	kein Ödem noch Präzipitate
+?4 4	0 4 (0 7)	98	0 ? (0 2)	0 7 (0 9)	1 0 (1 0)	5/4	+	Pigmentverschiebungen
+ 8 5	0 5 (0 7)	118	0 1 (0 2)	0 4 (0 9)	0 9 (1 0)	5/4	+	Pigmentverschiebungen

Die Zahlen in Klammern sind die Sehschärfewerte des gesunden normalsichtigen Auges Die Sofortadaptationskurven und die Blendempfindlichkeit die an den mit + versehenen Tagen aufgenommen wurden sind in Abb 1 dargestellt

uns waren im April/Mai und Oktober/November die meisten und im Dezember die wenigsten Erkrankungen zu verzeichnen signifikant waren die Unterschiede allerdings nicht

Die *Geschlechtsverteilung* ergibt mit 42 Mannern und 65 Frauen etwa das Verhaltnis von 2 3 die *Altersverteilung* (Abb 1) umfasst Patienten von 15 63 Jahren wobei die Erkrankungshaufigkeit gleichmassig ansteigt und nach einem Gipfel bei den 36 bis 40 Jahrigen wieder kontinuierlich zuruckgeht Eine Neuritis nervi optici ist sowohl bei Kindern als auch im hoheren Alter *selten* Lediglich Kennedy & Carroll beschrieben mehrere Beobachtungen bei Kindern bei denen eine grossere Tendenz zum bilateralen Auftreten starkere Begleitkopfschmerzen und uberwiegend die Verlaufsform als Papillitis zu beobachten war In der Regel tritt die Sehnervenentzundung zunachst nur an einem Auge auf und – falls uberhaupt – erst eine zeitlang spater auch am anderen Immerhin hatten von unseren Patienten aber doch 12 eine Neuritis nervi optici zu gleicher Zeit an beiden Augen

Symptome

Unter den subjektiven Symptomen spielen die Angaben uber *Sehstorungen* die grosste Rolle *So wurden von 89 unserer Patienten als Initialsymptom Schleier*sehen Verschwommensehen Schatten vor dem Auge oder Sehverschlechterung genannt wogegen bei den anderen 18 *Kopf und Augenschmerzen* als Druckschmerz oder ziehender Schmerz bei Blickbewegung im Vordergrund standen In diesen Fallen folgten Sehstorungen nach 1 bis 8 Tagen

Befunde

Ubereinstimmend mit diesen subjektiven Angaben war unter den objektiven Befunden fast immer eine mehr oder minder starke *Beeintrachtigung der Sehscharfe* vorhanden Nur 4 Patienten hatten auf dem erkrankten Auge noch eine



Abb 1
Altersverteilung von 107 Patienten mit Neuritis nervi optici

Tabel 6

Makulafunktion wahrend Verlauf der Retinitis zentralis serosa der Versuchsperson I(R A 33jahr Mann seit 3 Tagen Flimmern v d re Auge

Dat d Untersuch	Visus wahrd Sofortadapt	benotigte Zeit i sec	Blendungsempfindlichkeit Visus bei Beleuchtungsstufe			Visus an Sehproben tafel	Storungen am Amsler Netz	ophthalmoskop Befund
			1	8	64			
+30 1 69	0 0 (0 6)	–	0 0 (0 0)	0 0 (0 3)	0 1 (0 8)	5/10 +4 0 = 5/4	+	Makulaodem
+ 8 2	0 1 (0 6)	48	0 0 (0 0)	0 2 (0 3)	0 6 (1 0)	5/15 +2 0 = 5/4p	+	Makulaodem
12 2	0 0 (0 7)	–	0 0 (0 0)	0 0 (0 6)	0 6 (1 0)	5/15 +2 5 = 5/4p	+	Makulaodem
15 2	0 0 (0 7)	–	0 0 (0 0)	0 1 (0 9)	0 6 (1 0)	5/15 +2 5 = 5/4p	+	Makulaodem
19 2	0 0 (0 7)	–	0 0 (0 0)	0 0 (0 6)	0 3 (1 0)	5/15 +2 5 = 5/4p	+	Makulareflex unregelmassig Prazipitate d Retina
25 2	0 0 (0 7)	–	0 0 (0 0)	0 1 (0 5)	0 6 (1 0)	5/15 +2 0 = 5/4p	+	Makulareflex unregelmassig Prazipitate d Retina
4 3	0 0 (0 7)	–	0 0 (0 0)	0 1 (0 9)	0 5 (1 0)	5/20 +2 0 = 5/4p	+	Makulareflex unregelmassig Prazipitate d Retina
14 3	0 15 (0 6)	47	0 0 (0 0)	0 1 (0 9)	0 5 (1 0)	5/35 +2 0 = 5/7	+	Makulareflex unregelmassig Prazipitate d Retina

Aus der Universitäts Augenklinik Mainz
(Direktor Prof Dr A Vogel)

DIE NEURITIS NERVI OPTICI

VON

INGEBORG HEINRICH

Noch immer bringt das Krankheitsbild der Sehnervenentzündung (Neuritis nervi optici) von Fall zu Fall erhebliche diagnostische und therapeutische Probleme mit sich egal ob der papillenferne Abschnitt als Neuritis *retrobulbaris* oder der papillennahe Optikusanteil als Neuritis *intrabulbaris* = *Papillitis* befallen ist Wenn sich auch in vielen Fällen die Symptome spontan und schnell zurückbilden und oft sogar eine Restitution ad integrum erreicht wird so ändern sich doch in anderen Fallen Funktionsverfall und pathologischer Papillenbefund oft lange Zeit nicht und es kommt trotz Anwendung zahlreicher therapeutischer Massnahmen zu folgenschweren Defektheilungen

So steht der behandelnde Augenarzt eigentlich bei jeder Sehnervenentzündung immer wieder vor einer Reihe unbekannter Faktoren von denen einige vielleicht zu klaren sind wenn man ein grosseres Krankengut auswertet Dies soll im Folgenden geschehen

Eigenes Krankengut

Anamnese

Den Ausfuhrungen liegen anamnestische Angaben und Befunde von 107 Patienten aus den letzten 6 Jahren zugrunde In den einzelnen Jahren der Berichtszeit waren jeweils etwa gleich viele Patienten erkrankt

Einige Autoren hatten eine *jahreszeitliche Haufung* der Erkrankung z B im Fruhjahr (Miwa) oder in Vorfruhling und Herbst (Sugawara) gefunden Bei

Eingegangen am 20 Februar 1970

und Nover sehen die Storung des Licht und Farbensinns bei Retinitis zentralis serosa *als so charakteristisch an* dass sie eine wertvolle Hilfe bei der Diagnostik in Fallen von geringgradigem objektiven Fundusbefund zu *leisten vermag*

Die Prufung am Nyktometer wahrend des Erkrankungsverlaufes stellt nach unseren Befunden eine ahnlich empfindliche Methodik zur Beurteilung der Makulafunktion dar wie die Prufung des qualitativen Sehens am Amsler Netz

Zusammenfassung

Patienten mit makularen Veranderungen aber guter Sehscharfe wurden am Registrier Nyktometer des VEB Carl Zeiss Jena untersucht Dabei zeigte sich in 42 von 46 Fallen eine *Storung der Sofortadaptation die sich in herabgesetzter* Sehscharfe und verlangerter Adaptationsdauer äusserte oder sogar in volligem Verlust der Sofortadaptation

In 34 Fallen wurde eine erhohte Blendempfindlichkeit nachgewiesen

Daneben wird uber Nyktometerbefunde wahrend des Verlaufs von Retinitis zentralis serosa berichtet

Auf den Wert der Nyktometer Untersuchung als Funktionsprufung in Fallen von Makulaerkrankungen mit noch guter Sehscharfe beim Tagessehen wird hingewiesen

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krankung unabhängig fanden sich darüber hinaus einige Male degenerative Veränderungen im Maculabereich sowie arteriosklerotische diabetische oder hypertonische Gefässveränderungen

Bei unseren 107 Neuritis Patienten trat 93mal die Erkrankung zunächst nur einseitig auf 45mal war das rechte und 50mal das linke Auge betroffen 14 dieser Patienten bekamen später d h nach 4 Wochen bis mehreren Jahren eine Neuritis auch am anderen Auge Weitere 12 Patienten hatten – wie oben schon erwähnt – an beiden Augen zu gleicher Zeit eine Sehnervenentzündung *Zweimal traten Rezidiverkrankungen am selben Auge auf* einmal nach 3 Wochen einmal nach 3 Jahren

Ätiologie

Die eingangs erwähnten diagnostischen Probleme bei der Neuritis nervi optici betreffen vor allem die Klärung der Krankheitsursache Man fahndet nach durchgemachten Viruserkrankungen (Crippe!) bakteriellen Infektionen inter nen Krankheiten endokrinen Störungen und diskutiert vor allem die Beziehun gen zur Encephalomyelitis disseminata (Hyllested & Moller) Wir führten aus diesem Grunde bei unseren 107 Patienten insgesamt 320 konsiliarische Unter suchungen in anderen Fachkliniken durch (Abb 3) Wie oft sich dabei patholo gische Befunde erbagen geht ebenfalls aus der Abb 3 hervor Es wurde bei etwa jedem zweiten untersuchten Patienten im *HNO Bereich* ein pathologischer Befund meist eine Tonsillitis gefunden 12mal wurde daraufhin noch während der augenklinischen Behandlung eine Tonsillektomie durchgeführt Ähnlich häufig fanden sich Befunde bei Untersuchungen in der *Zahnklinik*

Da in der ophthalmologischen Literatur angegeben wird dass die Multiple Sklerose in 10 5% (Trzcinska & Kosowitz) bis 76% (Lynn) als Ursache der Sehnervenentzuundung infrage kommt wurden an diesbezügliche *neurologische Untersuchungen* besondere Erwartungen geknüpft Sie ergaben aber nur 21mal – also nur bei jedem Vierten der neurologisch untersucht wurde – etwas Auf fälliges Allerdings sind die aetiologischen Zusammenhänge zu Anfang oft schwer zu klären weil die Sehnervenentzündung den neurologischen Sympto men unter Umständen Jahre vorausgehen kann Im neurologischen Schrifttum wird die Multiple Sklerose in 33 3% als Ursache der Neuritis (Scheid Bradley) *genannt Brain hält nur die* einseitige Neuritis für eine Folge der Encephalo myelitis disseminata Bei unseren Patienten war eine solche 5mal zum Zeit punkt der Augenerkrankung zu sichern und 8mal wahrscheinlich zu machen In den anderen Fällen fanden sich Nikotin bzw Alkoholabusus (6 ×) Polioen cephalitis (1 ×) und Lues cerebrospinalis (1 ×)

Die *internistische Untersuchung* ergab 15mal pathologische Befunde doch kamen die meisten davon – abgesehen vom Diabetes – nicht als Ursache der Neuritis nervi optici infrage Bei 16 Patienten liess sich nirgendwo etwas Pa

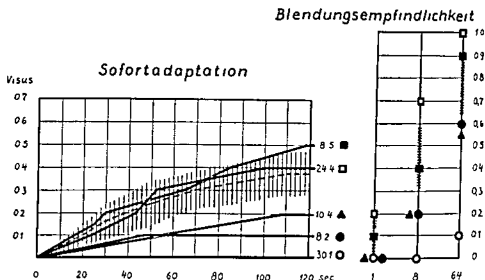


Abb 1

Sofortadaptation und Blendempfindlichkeit der Versuchsperson I wahrend des Verlaufs der Retinitis zentralis serosa des rechten Auges Zum Vergleich ist die Mittelwertskurve der Sofortadaptation (gestrichelte Linie) mit der Standard abweichung s (senkrechte Striche) die durch einmalige Untersuchung des rechten Auges von 20 normal sichtigen 30 39jahrigen Versuchspersonen gewonnen wurde mit eingezeichnet
Mittelwert und Streuung der Blendungsempfindlichkeit der gleichen Normalgruppe sind punktiert gezeichnet

Blendempfindlichkeit am 30 1 69 ○
8 2 69 ●
10 4 69 ▲
24 4 69 □
8 5 69 ■

höht Im Schrifttum wird meist über die Readaptationszeit das ist die Erholungszeit fur die Sehscharfe nach starker Blendung berichtet Diese ist bei makularen Erkrankungen nach Forsius Erigsson und Krause Henkind und Siegel Consul und Charan erheblich verandert und sie gilt nach Seferin Tour und Kershaw als scharferes Kriterium als die Sehscharfe

Nach unseren Ergebnissen erweist sich die Untersuchung am Registrier Nyktometer des VEB Carl Zeiss bei makularen Veranderungen als eine sehr empfindliche Funktionsprüfung Die Klagen der Patienten können besser objektiviert werden Damit findet das Gerat neben der Untersuchung zur Verkehrstauglichkeit (Broschmann) hier einen weiteren Einsatzbereich An unseren 4 wiederholt untersuchten Fallen von Retinitis zentralis serosa konnten wir feststellen dass sich die wahrend der Erkrankung sehr stark herabgesetzte Sofortadaptation wieder erholt Das konnten auch Jaeger und Nover bei Retinitis zentralis serosa in 4 Fallen am Nyktometer nach Comberg nachweisen Jaeger

normale Sehscharfe 52mal betrug sie weniger als 1/10 4 Augen waren bereits erblindet (Abb 2)

Keiner der Patienten hatte noch ein normales *Gesichtsfeld* Bei jedem zweiten Patienten waren zentrale parazentrale oder Ringskotome vorhanden bei den anderen bestanden Einengungen der Aussengrenzen und Ausfalle in der Gesichtsfeldmitte

Am *Augenhintergrund* hatten 43 Patienten bei Krankheitsbeginn einen normalen Papillenbefund als Ausdruck einer *retrobulbaren* Lokalisation der Neuritis Die Diagnose »Sehnervenentzündung« stutzte sich in diesen Fallen auf die nachweisbaren Funktionsstörungen In den ubrigen 76 Fallen war die Papille hyperaemisch oedematos unscharf begrenzt z T fanden sich Blutungen und Gefässeinscheidungen 18mal bestand eine Optikusatrophie Von der jetzigen Er

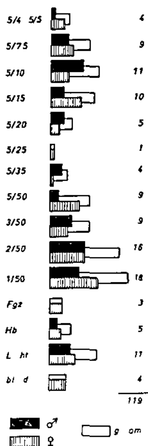


Abb 2
Visuswerte der erkrankten Augen bei Klinikaufnahme

From the Eye Department Hadassah University Hospital Jerusalem
and from the Neurosurgical Department
Hadassah University Hospital Jerusalem

ORBITAL HEMANGIOMA GROWTH DURING PREGNANCY

BY

HANAN ZAUBERMAN and MOSHE FEINSOD

Recurrent exophthalmos has been observed in orbital hemangiomata and explained on the basis of recurrent hemorrhages

The following report will deal with a case of recurrent exophthalmos beginning with puberty and exacerbated by pregnancy

Case Report

A 31 year old woman has suffered from a mild left proptosis since 1951 The condition remained stable until 1968 and repeated exophthalmometries showed readings of 18 mm in the right eye and of 20 mm in the left eye and visual acuities of 6 6 in each eye In December 1968 when the patient was in the fourth month of her pregnancy the left exophthalmos began growing and the patient attended the eye clinic with a complaint of increasing proptosis in the left eye and a mild blurring of vision.

The examination showed a visual acuity of 6/6 in the right eye and of 6/9 in the left eye The intraocular pressure was within normal limits Hertel s exophthalmometer showed readings of 18 mm in the right eye and of 25 mm in the left eye The left eye was displaced straight forward (fig 1) There was a mild limitation of abduction of the left eye but the patient did not complain of diplopia

The left fundus showed changes in the posterior pole consisting of edema and retinal striae from the disc to the macular area (fig 2) This area was 3 diopters higher than the surrounding parts of the fundus The right fundus was normal The left visual field presented an upper nasal quadrant c defect No neurological abnormalities were

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weist auf die Schwierigkeiten bei der einzuschlagenden Therapie und bei der Beurteilung der Prognose hin

Therapie

Aus diesen Grunden kann auch die Therapie der Neuritis nervi optici nur selten eine kausale sein Sie besteht in allgemeiner (Bettruhe) und ortlicher Ruhigstellung (Mydriasis Verband) und aus allgemein wie ortlich entgiftenden entzundungshemmenden roborierenden und durchblutungsfordernden Massnahmen Verwendet werden Irgapyrin Tomanol Tanderil als Injektionen Tabletten oder Suppositorien Cosaldon Complamin Niconacid als Tabletten Injektionen oder Infusionen Kalium jodatum Vitamin B Praparate Warme und unspezifische Reiztherapie (Schulz & Kment) (Abb 4)

Daruberhinaus wurden – vor allem bei akuten Verlaufsformen – fruhzeitig Cortisonpraparate (oral oder parenteral) gegeben in der Vorstellung rasch Entzundung und Exsudation zu unterdrucken und somit toxische Gewebsauswirkun

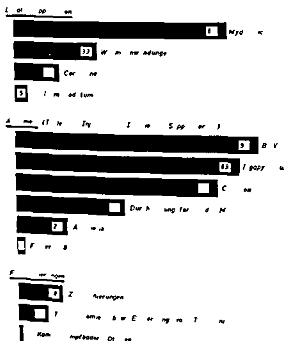


Abb 4
Behandlung bei Patienten mit Neuritis nervi optici

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13 *Neubauer H* Grundsatze der Lidchirurgie Klin Mbl Augenheilk 1965 *147* 313–335

Author s address Dr I Korchmáros Budapest VIII Mária u 39
II Szemklinika (Hungary)

To reconstruct slit canaliculi of any origin we start in the usual manner we make intermarginal incision on each lip between the skin and canalicular epithelium Then we unite the wound not by one and two sutures – as recommended in most textbooks – but by several U stitches and single sutures too (Fig 7) Otherwise the canaliculus may reopen (13) or get gaps which would hinder the normal outflow of tears

Summary

It was recommended a) different methods to find the torn end of the lacerated canaliculus b) the retrograd cannula to reconstruct the lacerated canaliculus to determine the site of the obstructed part of the canaliculus to make retrograde an artificial lacrimal punctum c) Hyasone own blood serum and cysteine to apply at probing for obstructed canaliculus d) a correct method to close the slit canaliculus

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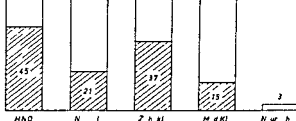


Abb 3

und Ergebnis 320 konsiliarischer Untersuchungen bei 107 Patienten mit Ne nervi optici

gisches finden 24 Patienten hatten dagegen mehr als einen krankha id 4 sogar 3

sucht man nun aus den vielen Einzelbefunden Ruckschlüsse auf logie der Augenerkrankung zu ziehen so kommen von den vielen M iten in erster Linie die Multiple Sklerose (13 ×) der Diabetes (6 ×) in Alkoholabusus (6 ×) die Lues cerebrospinalis (1 ×) infrage daz teren Fallen unmittelbar vorausgegangene Erkrankungen wie Zoster c icus Zahnextraktionen etc

nit war bei 31 Patienten also knapp 1/4 unseres Krankengutes die w liche Uusache der Sehnervenentzundung zu finden in 3/4 der Falle a einer Vielzahl pathologischer Befunde in anderen Fachgebieten ungek zumindest fraglich geblieben Dies liegt vor allem an der vorsicht pretation der in der HNO und Zahnklinik erhobenen Befunde

ch anderenorts wurde beobachtet dass im Gegensatz zu fruher Neb naffektionen viel seltener als Ursache einer Neuritis infrage kom et Calmettes Colli) Boros Wu Rucker Carroll Trzcinska Dabrowsk vicz geben in ihrem Krankengut 1/3 der Falle als aetiologisch ungek ei Cibis Otradovec & Votockova blieben es 50 % bei Nover 68 4 % a gar 75 % also ahnlich wie jetzt bei uns

se Zahlen hangen naturlich von Herkunft und Zusammensetzung des gen Krankengutes von der gerade vorherrschenden Lehrmeinung und oder minder subjektiven Deutung konsiliarisch erhobener Befunde ach bringt erst die Beobachtung des weiteren Krankheitsverlaufs Klaru ich dann wenn weitere Symptome im Laufe der Zeit hinzugekomn

merhin beleuchtet alles dies die eingangs aufgezeigte Problematik

The camera units of both instruments are fitted with a spherical and plar mirror and AGA Thermovision® with an optical system of lenses (germanium The object is scanned horizontally (rotating element) and vertically (oscillatir mirror) The incoming infrared radiation is focused on the detector which is a InSb crystal

The *display unit* is a modified oscilloscope (The signal from the detector preamplified and processed before being used to modulate the intensity of tl beam in the picture tube The beam sweeps across the tube face in a patter corresponding to the scanning pattern of the camera and this permits simu taneous viewing and recording A picture of horizontal lines is formed on th screen each line consisting of a certain number of dots The light intensity c each dot is proportional to the infrared radiation emitted by the specific poir investigated on the surface of the object) On the black and white picture thu produced, called grey tone picture the hot areas are portrayed in light shade of grey and the cool areas in darker tones

If isotherms are used these show up as white areas and this enables areas o identical temperatures to be easily distinguished Isotherms can be superim posed along the entire grey tone scale

Recording

The thermal picture displayed on the screen of the oscilloscope is photographed either with a polaroid black and white or a 35 mm colour film If filters of dif ferent colours are placed between the viewing screen and the colour film *i e* one for each isotherm and each colour is exposed on the same frame a thermal picture is produced on which temperature differences can be easily evaluated

In Table 1 the technical features of the two thermographs used are compared

A picture temperature range of 5° C and an isotherm width of 0 25° C (AGA Thermovision®) and 0 125° C (Bofors Infrared Camera) were used as stan dards In order to obtain maximum magnification the thermal picture was elec tronically expanded and thereby also the isotherm width Consequently one scale unit i e the distance between the first and the third mark on the scale was not equal to 1° C (For conversion into Centigrades the factor 0 75 should be used)

In the AGA Thermovision® the entire eye is portrayed if maximum magni fication is used For this reason each eye was examined separately The tempe rature levels of the eyes were kept constant by comparing the energy emitted by each eye with the energy emitted by an ambiant controlled temperature re ference

Absolute standardization of the experimental conditions was not possible but

dert und 16mal trat eine temporale Abblassung auf. Obwohl in diesen Fällen also eine Verschlechterung des Papillenbefundes eintrat, besserte bzw. normalisierte sich auch in der Mehrzahl dieser Fälle der Visus. Dieser scheinbare Widerspruch zwischen objektivem Papillenbefund und Funktion ist auch bei anderen Optikusprozessen zu beobachten, worauf u. a. Nover am Beispiel von Patienten mit Hypophysentumoren hingewiesen hat.

Prognose

Wie die Auswertung dieser Krankengeschichten zeigt, kann eine Sehnervenentzündung abheilen, ohne dass nachweisbare Schädigungen am Sehnerven zurückbleiben. Tritt im Laufe der Zeit eine Papillenabblassung auf, so muss dies nicht unbedingt auch mit einer Verschlechterung der Funktion einhergehen. In einigen dieser Fälle beobachteten wir eine Funktionsverbesserung, ja sogar eine Normalisierung. Prognose und Wiederherstellungsvermögen hängen von der Krankheitsursache und -dauer ab. Darüber hinaus spielt offenbar eine Gefässkomponente und das Lebensalter eine Rolle, denn bei jüngeren Patienten sind – wie es auch Farl & Martin fanden – die Endresultate besser als bei älteren.

Zusammenfassung

107 Patienten (42 Männer, 65 Frauen), die in den letzten 6 Jahren wegen einer Neuritis nervi optici stationär behandelt wurden, standen in einem Alter von 15 bis 63 Jahren. Der Erkrankungsgipfel lag bei den Männern zwischen 31 und 35 Jahren und bei den Frauen zwischen 36 und 40 Jahren. 12mal waren zu gleicher Zeit beide Augen befallen, 14mal erkrankte das zweite Auge einige Zeit später. Fast immer waren Sehstörungen das Initialsymptom und dementsprechend Visusminderung und Gesichtsfeldausfälle vorhanden. 76mal bestand ein pathologischer Papillenbefund.

Die Aetiologie liess sich nur in einem Drittel der Fälle klären, was an der Schwierigkeit liegt, die konsiliarisch in anderen Fächern erhobenen Befunde zu interpretieren. Eine Multiple Sklerose konnte 5mal gesichert und 8mal wahrscheinlich gemacht werden.

Die Therapie wird beschrieben; sie führte in einem hohen Prozentsatz zu einer Verbesserung der Funktion, auch dann, wenn ein pathologischer Papillenbefund verblieb. Die durchschnittliche Behandlungsdauer betrug 21,5 Tage.

Anschrift des Verfassers:

Dr. med. Ingeborg Heinrich, Univ.-Augenklinik, 65 Mainz, Langenbeckstrasse 1, BRD

eye the difference being statistically significant ($P < 0.01$) In 12 of the 18 cases the affected eye was warmer by 0 5 scale units or more than the healthy fellow eye As the optical and thermal resolutions are relatively small in the two thermographs used an elevated temperature of the affected eye was considered as abnormal only if the temperature difference between the two eyes was 0 5 or more scale units As the iridocyclitis subsided the temperature of the eye gradually decreased In view of the fact that hyperaemia of the pericorneal vessels and uveal tissue is associated with iridocyclitis this is not surprising

Fig 1 shows a histogram of the temperature difference between the affected eye and the healthy fellow eye The mean value of the difference is statistically significant ($P < 0.01$)

In 3 of the 6 cases in which a derivative of adrenalin was instilled in both eyes the temperature of the affected eye increased as compared with that of the healthy eye This drug causes constriction of the conjunctival and pericorneal vessels of the healthy eye and this results in blanching of the latter The pericorneal vessels lying at a deeper level are not affected in acute iridocyclitis The difference between the cases in which 10 per cent Neosynephrine® was instilled and those in which the drug was not applied was not statiscally significant

Out of the 5 cases of anterior uveitis associated whith posterior uveitis the affected eye was warmer by 0 5 scale units than the healthy fellow eye in 3 cases In 2 of these latter cases a mild anterior inflammation co existed which might have been involved in the elevated temperature In 1 of the 2 cases of choroiditis the affected eye was warmer than the healthy fellow eye

In the two cases of retrobulbar tumour the affected eye was warmer than the healthy fellow eye One of these patients had exophthalmus and the histological examination showed the retrobulbar tumour to be meningiom In the other case a pathological report was not available.

Out of the 5 cases of choroidal tumor the affected eye was warmer than the healthy fellow eye in 3 cases In one of these latter cases the histological examination showed the tumour to be a malignant melanoma and in the other two cases a pathological report was not available Out of the remaining two cases of the former group one patient had only one eye the fellow eye having previously been enucleated In the other case in which there was a metastatic mammary carcinoma to the choroid the healthy eye was warmer than the effected eye

In 3 cases of tumour of the iris cornea and choroidea respectively the tumour could not be portrayed thermographically This was rather surprising particularly with regard to the choroidal tumour as the latter was relatively large infiltrated the ciliary body and appeared to be malignant. The probable reason was that the magnification was insufficient and the optical and thermal resolutions were too small in the thermograph

gen und das Oedem des Opticus zu beseitigen und den Druck von den Sehnervenfasern zu nehmen

Die Applikation erfolgte als Stosstherapie mit einer Anfangsdosis von 60 bis 80 mg in der Regel kam es auf eine Gesamtmenge von 450 bis 500 mg in einzelnen Fallen in denen eine MS *gesichert war aber auf erheblich mehr* weil eine Langzeitbehandlung notwendig war Im ubrigen variierten wir die Dosis je nach dem Grad der Visusminderung

Zahlreich sind in der Literatur die Arbeiten die sich mit der Wirksamkeit (Neubauer & Karges, Doden Yokoyama, Kaneko Nakai & Taniguti) bzw Unwirksamkeit (Kazdan & Kennedy, Rucker Giles & Isaacson Oksala Angstwurm & Frick Glatzel & Lungershausen) der Nebennierenrindenhormone bei Neuritis nervi optici befassen Ein abschliessendes Urteil ist insofern schwer moglich als fast immer auch gleichzeitig andere Medikamente gegeben werden und gar nicht selten auch Spontanheilungen vorkommen Entscheidend ist der fruhzeitige Behandlungsbeginn in den ersten 10 Tagen doch lässt sich auch dann die Erkrankungsdauer nicht signifikant kurzen (Graeber)

Behandlungsdauer

Die Dauer des Klinikaufenthaltes betrug bei unseren 107 Patienten durchschnittlich 21 5 Tage (bei Graeber 26 28 Tage bei Nover 22 Tage) im kurzesten Fall 6 im langsten 92 Tage weil es zu Rezidiven gekommen war

Verlauf

Der Verlauf einer Neuritis nervi optici lässt sich am besten aus dem Vergleich der Befunde bei Krankheitsbeginn und ende beurteilen Soweit es die *Sehscharfe* betrifft (vergl Abb 2) hatten und behielten 4 Patienten eine normale Sehscharfe Bei den ubrigen 115 Augen bestand eine mehr oder minder ausgepragte Visusminderung die in 2 Fallen noch zunahm 5mal unverandert blieb und sich in *90 % besserte Insgesamt 57 14 % verliessen die Klinik mit normaler* Sehscharfe

Ahnlich verhielt es sich mit den *Gesichtsfeldausfallen* die in keinem Fall grosser wurden 106 der 119 Neuritisfalle hatten bei Klinikentlassung wieder normale Aussengrenzen 1/3 hatte keine zentralen Ausfalle mehr in 65 Fallen waren sie kleiner geworden

Von den 43 unserer Neuritisfalle die bei Klinikaufnahme einen regelrechten *Papillenbefund* hatten bekamen 10 trotz aller Behandlung doch noch eine temporale bzw totale Atrophie die anderen 33 blieben unauffallig Die bei 18 schon zu Beginn vorhandene Papillenabblassung (16mal temporal 2mal total) änderte sich während des Klinikaufenthaltes nicht Der Papillenbefund der ubrigen 58 normalisierte sich *15mal* besserte sich *20mal* blieb *7mal unveran*

In 2 of the 5 cases of choroidal neoplasm histological examination showed the tumour to be malignant In 1 case malignancy was suspected because the patient had a history of enucleation of the fellow eye on account of malignant *choroidal tumour which had been confirmed histologically* In the other 2 cases a pathological report was not available

All these patients were examined by thermography In 37 patients only one eye and in the other both eyes were affected Eleven of these 38 patients were examined by thermography on several occasions

Twenty patients were examined in a sitting posture 10 of these without a mirror and the other 10 patients prone with a mirror suspended in front of them and angled at 45° From this mirror the radiation coming from the eye is reflected into the camera The other 18 patients were examined prone under anaesthesia after the application of a blepharostat and the instillation of an in different volatile solution This was done to avoid dessication of the cornea These latter patients were examined with a mirror which was suspended in front of them and angled at 45° Twenty patients kept their eyelids apart spon *taneously*

In 5 of these 18 patients the anaesthetic was tetracaine combined with the instillation of physiological NaCl in 2 and Isopto Plain in 3 patients In the other 13 cases anaesthesia was produced with Novosin and was combined with the instillation of Methocel * at intervals from 5 to 10 minutes In 4 cases the examination was carried out both with and without a blepharostat In 6 cases the patient was examined after the instillation of an adrenalin deri vative

Forty one patients with healthy eyes were identically examined and were used as controls Twelve of them were examined in a sitting posture without a mirror *On the other 29 patients the examination was carried out with* the pa tient prone and a mirror placed in front of them In 4 of these latter cases a blepharostat was used

Results

Table 2 shows the temperature difference between the affected and healthy eye in the 38 cases in this series the difference being expressed in scale units

In the 18 cases of unilateral acute iridocyclitis the following *observations* were made In 14 of them the affected eye was warmer than the healthy fellow

---

* Isopto Plain® (5 mg/ml) *Alcon Universal Ltd Fort Worth Texas* U S A

** Novosin® (0 4 %) Dr A Wander A G Bern Schweiz

*** Methocel® (2 %) Dr E Breschlin A C Winterthur Schweiz

Universitätsaugenklinik Aarhus
(Chef: Professor Viggo A. Jensen)

MIT DER HAND BEDIENTES SCHALTPULT ZUM MOTORISIERTEN OPERATIONSMIKROSKOP MODEL II DER FIRMA CARL ZEISS, OBERKOCHEN

VON

VIGGO A. JENSEN

Das Schaltpult, welches normalerweise zum motorisierten Operationsmikroskop Modell II der Firma Carl Zeiss gehört, muss unter dem Behandlungstisch angebracht und vom Chirurgen am besten in sitzender Stellung mit den Füssen bedient werden. Nach meinen Erfahrungen ist das Schaltpult etwas umständlich und unbequem und mit den Schuhen, wie man sie in Operationszimmern benutzt, schwierig zu bedienen. Ausserdem kann der Kardan-Aufhang des Mikroskopes nicht vollständig ausgenutzt werden, da der Chirurge an seine Stellung am Behandlungstisch gebunden ist und sich nicht fort bewegen kann, ohne die Fühlung mit dem Schaltpult zu verlieren.

In Zusammenarbeit mit dem dänischen Vertreter der Firma Zeiss, die Firma Brock & Michelsen in Kopenhagen*, ist es gelungen ein kleineres Schaltpult zu konstruieren, das mit Hilfe von Tasten, auf die man mit den Fingern drückt, bedient wird, wodurch es möglich ist selbst ganz kleine Korrekturen von sowohl Höheneinstellung, dem kontinuierlichen Ändern der Vergrösserung, der Fokusierung und der automatischen Mitteneinstellung von letzterer vorzunehmen. Wie aus der Abbildung hervorgeht, ist an der linken Seite des Mikroskopaufhanges mit Hilfe einer gewinkelten Platte und 3 Bolzen eine viereckige Metallkassette (12 × 18 × 5.5 cm) angebracht. Von den 7 Jautz Drucktasten wirkt jede auf ihren Burgess Mikroumschalter. Sie sind mit anderen Federn ausge-

* Brock & Michelsen, Vestergade 43 25, 1456 Kopenhagen K.

Eingegangen am 9. Februar 1970.

Disease	No of Cases	Patients Record No	Date of Examination	Affected Eye	Healthy Eye
			? 5	+ 1 7(2)	+ 1 8
			7/5	+ 0 1( )	+ 0 4
		S V 981008	4 ?		+ 0 ?5
			ı/2		+ 1 5
Anterior Associated with Posterior Uveitis	5	H C 480710	5/3	+ 0.5	
		O A 150913	12/3		+ 0 6
		S L 420302	12/3	+ 0 7	
			20/3	+ 0 5	
		E S 450410	20/3		+ 0 4
		W L 090714	29/4	+ 0 6	
Choroiditis	2	I P 491017	27/2		+ 0.3
			3/3	+ 0 1	
			7 3		+ 0 1
			10/3		+ 0 4
		K E 400/03	29/4	+ 0.5	
Choroidal Tumour	5	T B ??1029	9/1		+ 0 4
		J M ?60711	?8/2	+ 0 4	
		G S 310222	29/4	+ 0 5	
		F B 021013	23/4	+ 0 3	
		B K 021228	4 5		Prothesis
Retrobulbar Tumor	?	O E 110828	19 3	+ 1 0	
		O M 1104?0	16/4	+ 0 5	
Contusion of the Eyeball + Iridodialysis	1	H M 540120	29/1		+ 1 0
Episcleritis	1	L C 510?07	24/2		+ 0 1
Panophthalmitis	1	W F 060730	24/1	+ 0 7	
Bilateral Central Retinitis Left eye more affected than right eye	1	L I 060/ 7	5/2	+ 1 2	
			7/2		+ 0 4
Tumour of the Iris	1	C M 4/0315	7/3		+ 0 2
Tumour of the Cornea (Histologically confirmed malignant Melanoma)	1	K L 060?24	14/4		+ 0 4

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Table 2

Temperature Difference[1] between Affected Eye and Healthy Fellow Eye in the 38 Cases in This Series

Disease	No of Cases	Patients Record No	Date of Examination	Affected Eye	Healthy Eye
			1968		
Acute Irido cyclitis	18	D A 370312	18/12	+ 1 2	
		H A 170416	18/12	+ 2 0	
			1969		
		B S 450810	24/1	± 0	
			28/1	+ 0 2	
		L E 090321	2/3		+ 1 0
			3/3		+ 0 2
			6/3		+ 0 9
		L B 290830	27/2	+ 1 0	
			3/3	± 0 4	
			5/3	+ 0 5	
			6/3	± 0	
Recurrence			12/3	+ 2 5	
			24/4	+ 0 5	
			28/4	+0 5 +1 0[2]	
		K I 060501	7/3	+ 0 1	
			13/3		+ 0 9
		S H 270225	27/2	+ 1 0	
			6/3		+ 0 4
			13/3		+ 0 4
		S M 571125	5/3	+ 1 0	
			7/3	+ 0 3	
			12/3	± 0	
		A S 441205	4/2	+ 0 3	
		E T 300919	7/2	+ 0 5	
		N S 150504	25/3	+ 0 7	
		W E 441025	16/4	+3 5 +2 8[4]	
		S B 290604	22/4	+1 0 +0 5( )	
			28/4	+1 3 +0 8( )	
		O B 441027	17/4	+1 0 +2 5[3]	
			22/4	+0 5 +0 5( )	
		M M 450112	30/4	+2 0 ±0( )	
			2/5	+0 , +0 5( )	
			7 5	+0 7 +0 5[2]	
		L V 460712	16/4	+ 0 3	
		A H 051019	28/4		+0 3 +0 3[2]

(1) = Expressed in scale units
(2) = Neosynephine® (10 %) Winthrop Products Co Winthrop
(3) = Neosynephine® (2 5 %) House Surbiton on the Thames England
(4) = Eppy® (1 %) Pharmacia AB Bjorkgatan 30 Uppsala Sweden

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THERMOGRAPHY IN THE DIAGNOSIS OF DISEASES OF THE EYE AND THE APPRAISAL OF THERAPEUTIC EFFECTS

A Preliminary Report

BY

LILLEMOR WACHTMEISTER

Introduction

In the last 40 years thermography has been increasingly used for industrial and military purposes but only in the last 10 years have a few workers recognised its usefulness in the field of medicine (*Lloyd-Williams et al* 1963 *Gershon Cohen et al* 1965 *Bowling Barnes* 1965 *Notter & Melander* 1968)

Every object exchanges energy with its environment and maintains thermal equilibrium with the latter by constantly absorbing and emitting electromagnetic energy such as infrared radiation which is a function of its temperature Thus every object whose temperature is above absolute zero spontaneously emits and absorbs infra red radiation

If electromagnetic energy (E) strikes a partly transparent object E is equal to T + A + R T A and R expressing the object s transmission absorption and reflexion in per cent If the object is a mirror E is equal to R and A and T are very small It the entire object is transparent, T approaches 100 and R and A are small If the object is opaque E is equal to R + A and T is equal to zero If the object is opaque with a roughened or blackened surface T is equal to zero R being small and E being equal to A Absorption of energy

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two eyes in the control group The results being expressed n scale units The controls were divided into five groups according to the temperature difference It is seen that the difference between the two eyes ranged form 0 0 5 scale units but in a few cases it exceeded 0 5 scale unit

Fig 2 shows a histogram of the temperature difference between the right and left eye in the control group The mean value of the difference is not statistic ally significant ($P > 0\ 20$)

Discussion

Pourjat (1966) observed that the temperature over inflammatory processes and tumours behind the eyeball was elevated in exophthalmos but if the latter was due to other causes it was not elevated His series included 1 case of carotico – cavernous fistula in which the affected side of the face was cooler than the healthy side He concluded from this observation that this was due to shunting of blood from the external to the internal carotid artery

From the observations made in a comparatively large series of cases of main

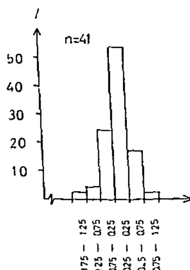


Fig 2

Histogram of Temperature Difference between the Two Eyes in the Control Group
x coordinate axis shows the difference between the two eyes expressed in scale units
y coordinate axis shows the precentage frequency

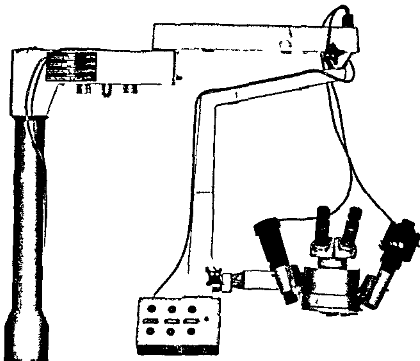


Fig 1

stattet sodass sie auf den leichtesten Fingeraufdruck reagieren Die 3 obersten Knopfe bewirken dass sich das Mikroskop nach Oben bewegt sowie grossere Vergrosserung und Fokusierbewegung aufwarts wahrend die 3 untersten Drucktasten entgegengesetzt wirken Wahrend der Operation ist die Vorderseite der Kassette mit einem sterilen durchsichtigen Plastikstuck das mit Heftpflaster befestigt ist zugedeckt

Die Handsteuerung ist fur die jungeren Kollegen eine grosse Hilfe da sie hierdurch mit der Anwendung des Operationsmikroskopes schnell vertraut werden

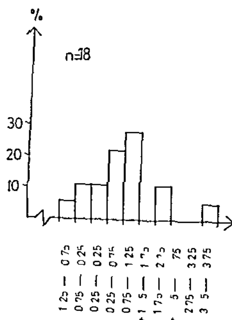


Fig 1
Histogram of Temperature Difference between Affected Eye (Iridocyclitis) and Healthy Fellow Eye
x coordinate axis shows the temperature difference between affected and healthy fellow eye expressed in scale units y coordinate axis shows the percentage frequency

In the case of bilateral central serous retinitis the eye which was more severely affected was warmer by 1 2 scale units then the fellow eye In the case of panophthalmitis the affected eye was warmer by 0 7 scale units than the fellow eye On the other hand in the case of episcleritis the healthy eye was warmer than the affected eye

Table 3 shows the distribution of the difference in temperature between the

Table 3
Temperature Differences(1) between the Two Eyes in the Control Group

Control group	Right eye		No difference	Left eye	
No of cases 41	> + 0 5	≦ + 0 5	± 0	≦ + 0 5	> + 0 5
Frequency	1	12	12	12	4

(1) = Expressed in scale units

and thermistors photometer (thermal effect) were used but today the leading material is indium antimonide (photoconductive and photovoltaic effect) which is cooled by liquid nitrogen and is sensitive to about 5.5 μ For infrared radiation of longer wavelengths detectors such as germanium (Ge) detectors doped in Hg Cu or Zn are required The doped detectors have to be cooled by neon or helium and this is associated with practical difficulties

For infrared photography IR filters and infrared films are required

Thermography has been reported to be an important tool to supplement other means of detecting and following up diseases within the fields of plastic surgery neurology rheumatology and internal medicine (malignant tumours burns and vascular diseases)

Whipple reviewed the medical potentials of thermography at the Symposium held in New York in 1964 *Pourjat* (1966) wrote that the eye was not suitable for examination by the infrared camera (Barnes Model M Thermograph System) available at that time because the temperature gradients were too small the magnification was insufficient and the scanning time was too long

Aarts (1969) discussed the applicability of this method to medical problems

With the exception of *Gross et al* (1967) and Keeney & Guibor who in 1969 reported at the Conference held at Wills Eye Hospital in Philadelphia on the usefulness of thermography in vascular and malignant diseases of the eye and in other soft tissue pathology thermography has so far not been used in ophthalmology to the best of author s knowledge

The recent improvments in the technique of thermography prompted the idea to investigate the value of thermography in the diagnosis of diseases of the eye and the appraisal of therapeutic effects

Method

Two different types of camera were used i e the * AGA Thermovision® and the Bofors Infrared Camera Basically both types operate identically but they differ in technical detail Each instrument has an indium antimonide detector which is cooled by liquid nitrogen and which is sensitive to wavelengths ranging from approximately 1 μ to 5 5 μ

The AGA Thermovision® has a shorter scanning time but the optical and thermal resolutions are slightly inferior to those of the Bofors Infrared Camera if theoretical specifications are compared Both are equipped with a *camera unit* and a *display unit*

AB AGA Lidingo I Sweden.

AB Bofors 690 0 Bofors, Sweden.

many tumours in which thermography enable the differential diagnosis between malignant and benign tumours to be made (*Melander & Notter* 1968) *Keeney & Guibor* (1969) concluded that this should also be possible in cases of tumour of the eye The latter workers also expressed the view that thermography should enable one to determine whether lesions such as exophthalmos were due to an endocrine disturbance or to inflammatory processes In the majority of the cases of malignant melanoma and retinoblastoma in their series the affected eye was warmer than the healthy fellow eye

The thermal picture produced in the thermographs used in this investigation was too small to permit a detailed study of the eye to be made However in cases of inflammatory processes in the eyeball and tumours in and behind the eye both instruments proved to be helpful in revealing the condition and ap praising the therapeutic effects

Improvements in some technical features particularly in the magnification of the thermal picture and the thermal and optical performances are required before thermography can be used as a routine method of examination in oph thalmology

Summary

Thirty eight patients with unilateral or bilateral diseases of the eye were examined by thermography using the AGA Thermovision® and the Bofors In frared Camera respectively

Forty one subjects with healthy eyes were identically examined and were used as controls

It was found that in cases of unilateral acute iridocyclitis anterior uveitis associated with posterior uveitis choroiditis retrobulbar tumour and choroidal tumour the affected eye was on average warmer than the healthy fellow eye

Improvements in some technical features of the instruments particularly in magnification of the thermal picture and the thermal and optical performances may lead to thermography becoming a useful tool to supplement the current methods used for detecting ocular diseases

Acknowledgments

Thanks t the courtesy of Messrs AB AGA Lid ngo Sweden, and AB Bofors Bofors wh kindly made the r thermographic apparatuses ava lable to me it was possible to carry out this invest gation Th s was of great value to me and I wish to extend my sincerest thanks to them for their generosity and invaluable co operation

causes the object s temperature to be increased and this total increase is eliminated through the process of emission as conduction and convection are negligible (*Bowling-Barnes* 1963)

The emission of electromagnetic energy is a fundamental phenomenon in Nature The total radiant energy (E) emitted by an object is directly proportional to its radiation efficiency factor called emissivity (ε) and its absolute temperature (T) This may be expressed by the formula $E = \varepsilon\ T^4\ \sigma$ where σ is the Stefan Bolzman constant = 5 673 × 10^{-1} watt cm^{-} × $K^{\circ -4}$ (*Bourjat* 1966)

Hardy (1939) demonstrated that human skin emits infrared energy in the wavelengths of approxamitely 3 μ to 30 μ with a maximum at about 10 μ He expressed the view that skin may be compared to a perfect emitter called a "black body" whose reflexion and transmission approach zero and peak energy absorption occurs

The emissivity of human skin water plastics and highly polished metallic surfaces in the infrared part of the spectrum has been given to be about 0 99 0 98 0 91 and 0 02 0 03 respectively The radiation efficiency factor is dependent on factors such as the structure and physical characteristics of the object s surface (*Bowling-Barnes* 1963)

The emissivity (ε_e) of the eyeball was determined by two different methods in 20 cases indirectly by estimating the reflexion coefficient (ϱ_e) in 10 cases and directly by appraising the emissivity (ε_e) in the other 10 cases According to these preliminary measurements the mean value of the emissivity was 0 9 (0 92 0 99) as determined by the indirect method There was no noteworthy difference between the eyeball and the skin with respect to emissivity This also showed that reflexion and the individual differences were neglibile

The corresponding figures as determined by the direct method were 0 8 (0 69 0 89) Thus the danger of extraneous factors influencing the results or misinterpreting the thermal picture can be considered small Further studies of the emissivity of the eyeball are in progress

The radiation of heat produces a pattern which can be portrayed by a thermograph The thermal pattern is influenced by loss of heat convection conduction radiation and evaporation Thus factors such as vascular and metabolic disturbances and the temperature of underlying structures and pathological processes of the skin also influence the thermal pattern *Melander & Notter* (1968) have shown that the human body can be chilled to a depth of 3 to 4 cm in an ambiant temperature of 23° C and that the chilling increases towards the surface of the body the temperature gradient being 5° C

The technique of thermography has been greatly improved in the last few years and different types of detectors have been used the aim being to shorten the detection time as much as possible without affecting thermal or optical performance Formerly cholesterol crystals (liquid crystal detector) thermally sensitive phosphors (phosphor effect) differential evaporation (evaporography)

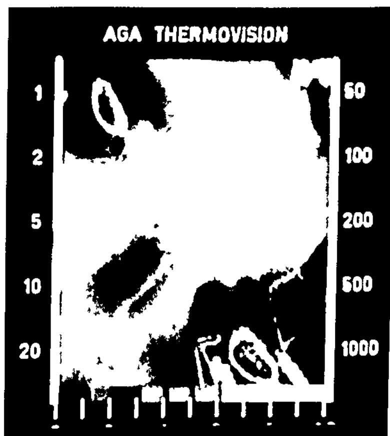


Fig 3

Coloured thermogram AGA Thermovision® derived from a case of iridocyclitis of the left eye The temperature range was 5° C and the isotherm width about 0 4° C The violet area in the left upper corner and the dark green area in the lower right corner represent the affected left eye and the healthy fellow eye respectively The former was 1 0 scale unit warmer than the latter

Table I

Comparison of the Technical Features of the AGA Thermovision with those of the Bofors Infrared Camera

Technical Data	AGA Thermovision® 669	Bofors Infrared Camera
Rotating element	Prism	Mirror drum
Frame rate	16	4
Thermal discrimination Two black body areas at romm temperature can be separated	0.2°	0.1–0.2°
Optical resolution	2 mrad 0.5–0.8 mm²	1.7 mrad 0.25–0.42 mm²
Number of lines per frame	100	125
Number of dots per line	100	125 (expanded picture)
Sensitivity	2.0–5.5 μ	1–5.5 μ
Magnification used	1:1	1:2
Distance	0.5 m	0.3 m

each eye of each patient was examined under identical conditions with respect to loss of heat evaporation and any existent air current in the examination room The ambiant temperature ranged from 21° C to 24° C the relative humidity from 21% to 32% and the atmospheric pressure from 756 mm to 761 mm Hg

Case Material

This series included 38 patients who were admitted to this Department with the following diagnosis unilateral acute iridocyclitis (18 cases) anterior uveitis associated with posterior uveitis (5 cases) choroiditis (2 cases) choroidal tumour (5 cases) retrobulbar tumour (2 cases) episcleritis (1 case) panophthalmitis (1 case) contusion of the eyeball associated with iridocyclitis (1 case) tumour of the cornea (1 case) tumour of the iris (1 case) and bilateral central retinitis (1 case)

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Vanersborg Sweden

ANISOMETROPIA AMBLYOPIA INDUCED ANISEIKONIA AND ESTIMATED CORRECTION WITH ISEIKONIC LENSES IN 4 YEAR OLDS

BY

W NORDLÖW

The study described in this paper is intended to determine if better final visual acuity in the most ametropic eye in anisometropia is obtained by early correction with iseikonic lenses rather than with conventional lenses If this is the case it will also be shown if a symptom caused by aniseikonia namely a retarded development of the visual acuity occurs and a method of treatment would be provided

Sight testing of 2937 randomly selected 4 year old children comprising 48 % of 4 year groups in a representative Swedish population revealed that there was a reduction of visual acuity related to refractive errors in one or both eyes in 6 4 ± 0 40 % Children with squints were not included in the material Following full correction with conventional lenses for 3 years 1 33 ± 0 211 % of the children still had a visual acuity of less than 5/5 in one or both eyes Among the 35 remaining cases there were 19 with anisometropia (with or without astigmatism) of 2 dioptres or more Among the 139 cases who had a visual acuity of 5/5 there were 2 children with anisometropia of the above amount The difference is significant ($P < 0\,001$) and shows that correction of anisometropia of 2 dioptres or more with conventional lenses even at the age of 4 does not ensure the development of normal visual acuity *W Nordlöw & S Joachimsson* (1966)

In order to explain the absent or partial improvement of the visual acuity in anisometropia of 2 dioptres or more with full correction by conventional

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ELECTRON MICROSCOPIC DEMONSTRATION OF VIRUS PARTICLES IN HUMAN HERPES SIMPLEX KERATITIS*

A study with special reference to macroscopically undamaged areas of the corneal epithelium

BY

SVEN ERIK G. NILSSON

In dendritic keratitis the corneal epithelium generally shows one or more lesions easily recognized in the slit lamp microscope. In severe cases the cells lining such lesions often contain large numbers of newly formed virus particles closely packed to crystalline-like bodies. These bodies might be visible in the light microscope as intranuclearly located inclusion bodies. However, if only scattered virus particles are present, electron microscopy is required for identification.

The ultrastructural features of herpes simplex virus are known from studies of inoculated chorioallantoic membranes and tissue cultures (6, 10, 13, 15, 19) and from experiments using negative staining techniques (20).

Intranuclearly located particles of the same appearance have been demonstrated in electron micrographs of rabbit corneal epithelium inoculated with herpes simplex virus (7, 17, 18). However, no systematic studies have been done. An attempt to study human herpetic keratitis was made by Takemura (16). Particles which are likely to be virus particles were seen intranuclearly, in the cytoplasm and extracellularly. Due to difficulties in connection with biopsy

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Table 5

Improvement of vision in 15 anisometropes who used full corrections with conventional lenses and iseikonic lenses for 2 3 years (Group B)

Observ time in years	No of eyes			Visual acuity							
	Not Examined	Examined									
		Worst	Best	5/5	5/6	5/10	5/15	5/20	5/30	5/50	4 1/50
0		15*					1	2	4	4	4
0 5		15				9	2	1	2	1	
1	1	14		1	1	9	2		1		
2		15		2	10	1	1		1		
3	3	12		6	3	2			1		
0			15*	10	2	2			1		
0 5			15	12	3						
1	1		14	13	1						
2			15	15							
3	3		12	12							

* Without correction lens

Zeiss stereo pictures it is known that a certain number have difficulty in appreciating the pictures This is usually achieved after some practice

Discussion

Two similar materials of 4 year olds with anisometropia of 2 dioptres or more and representative of a Swedish population have been treated with full correction of the refractive error Group A and B Group B has furthermore been given iseikonic corrections estimated for the anisometropia The visual acuity in this group after three years is significantly better than in Group A The induced aniseikonia which results from correction of anisometropia with conventional lenses is thus revealed as inhibiting the development of the visual acuity even to the extent of loss of central fixation in some cases This is thus an objective and measurable sign of aniseikonia Earlier publications have been mainly concerned with the subjective symptoms of aniseikonia disregarding those cases in which it has been possible to show a measurable improvement of binocular

selected groups of normal cases and patients have been examined *H F Gillott* (1950 1951) examined 100 specially selected cases in the age groups 8 75 years representative of the population He found that 42 % had aniseikonia of more than 0 8 % and 7 % of the group had more than 3 % In 280 Flight Cadets *A M Hicks* (1943) found aniseikonia < 0 5 % in 85 % and not more than 1 % in the remainder Corresponding results for *H Burian* (1950) among 107 Flight Cadets were 93 % and 7 % *P Boeder* (1950) reported that the studies suggest that the frequency of aniseikonia of clinical importance is low

In order to assess the clinical importance of aniseikonia groups of patients with asthenopic symptoms such as tiredness and headache have been examined Thus subjective symptoms are involved The patients have been treated initially with conventional lenses and prisms without or with bad results After the demonstration of aniseikonia this error has been corrected with an iseikonic lens *C Berens & M Loutfallah* (1939) obtained improvement of the symptoms in 68 % of 418 cases *A M Hicks* (1943) in 48 % of 86 cases *B Cushman* (1945) in 71 % of 24 cases *J P Macnie* (1948) studied 463 cases and found improvement in 79 % after 3 to 6 months and in 50 % after 5 to 10 years *R E Bannon* (1939 1949) and *H F Gillott* (1957) have shown that suppression poor fusion amplitude and poor stereopsis *all objective findings when occurring with aniseikonia can be improved and rendered normal in certain cases by correction with iseikonic lenses*

Furthermore *there is one factor to consider in the correction of meridional* aniseikonia There appears *in the space eikonometer a measurable declination* error which causes erroneous space perception *K N Ogle & I F Madigan* (1945) *H Burian & K N Ogle* (1945) found that the calculated and observed declination error usually coincided sometimes partly and sometimes not at all After correction of astigmatism with iseikonic lenses and allowing for the declination error and 9 months to 2 years observation time 85 % of 61 cases were more or less improved The above studies show that asthenopic symptoms with aniseikonia can be abolished or alleviated with iseikonic lenses in 50 80 % and binocular vision can be improved in certain cases

Measurements of aniseikonia in pre school children is not possible with current methods According to Bannon the children must be at least 6 years of age and have reached sufficient maturity see at least 20/60 in the worse eye and have binocular vision *A P Berte & K A Harwood* (1961) consider that children should be older than 6 years see 6/12 and have binocular vision in order to perform the examination The Eye Clinic of the Dartmouth Eye Institute introduced the idea that in the absence *of the measured value* a calculated (empirical) correction of the aniseikonia could be used *in the correction of anisometropia* (cit *Davis* 1959) This method should be applicable to *pre school children* to prevent suppression and amblyopia However there are difficulties *in* forecasting the degree of aniseikonia in relation to the degree of anisometropia

vision after iseikonic correction The results of the examination also indicate that aniseikonia has clinical relevance in the development of visual acuity when it reaches a degree which corresponds to a correction of anisometropia of ? dioptres or more

In spite of the fact that all over iseikonic corrections have been used the results have been very good It probably means that meridional aniseikonia which occurs when astigmatism is corrected is of lesser importance In Group B the astigmatic difference between the both eyes has been under 2 dioptres in all cases thus there is no data concerning greater differences In Group A there were ? cases with astigmatic differences greater than 2 dioptres *R J Davis* (195?) proporsal that astigmatism in children should always be corrected with estimated meridional iseikonic lenses should therefore be regarded with certain reservations

The results from Group A might suggest that it would be reasonable to await the estimation of the visual acuity after half a year of correction with conventio l lenses before assessing the prognosis for visual acuity If a visual acuity of 5/15 is then taken as the upper limit for correction with iseikonic lenses it should be remembered that a few cases with a poorer prognosis may be over looked Also valuable time is lost when the development of visual acuity is most amenable to favourable influences The results of iseikonic correction in this work are the result of starting treatment as soon as the anisometropia has been diagnosed

Conclusions

1 Full correction of anisometropia of 2 dioptres or more in 4 years olds gives an induced aniseikonia which *inhibits the development of visual acuity* demonstrable in 2/3 of cases This is thus an objective result of aniseikonia

? An all over iseikonic correction of 0 75 1 25 % per dioptre in 4 year olds gives significantly better visual acuity and mitigates against the development of eccentric fixation

3 Ommission of correction with meridional iseikonic lenses of astigmatic differences of less than 2 dioptres between the two eyes seems to be less important

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lenses an induced aniseikonia may be postulated The resulting difference of size or form of the images of the two eyes could impede the development of visual acuity in the more ametropic and already amblyopic eye By comparing the results of treatment in the material referred to above with a material col lected similarly and derived from the same area of 4 year old anisometropes from other years which also had correction with iseikonic lenses it would be possible to assess the importance of aniseikonia in the development of visual acuity

Review of the Literature

Between the years 1932 1945 Ames and his co workers at the Dartmouth Eye Institute studied in detail theoretically and clinically the differences in size and shape of the images of both eyes The difference between the images of both eyes which depends on the right and left eye viewing a fixed object from slightly different angles is called physiological It is necessary for binocular stereoscopic vision The non physiological difference is called anomalous ani seikonia It may be optically or anatomically determined The first may be a a function of the factors which determine the refraction of the eye or be in duced by correction of refractive errors Aniseikonia may occur in isometropia Thus *A M Hicks* (1943) found 24 isometropes among 86 cases with aniseikonia *A Berte & K Harwood* (1961) consider that correction of anisometropia is the most common cause to induced aniseikonia Anatomic aniseikonia may develop for example with varying densities of the sensory cells in the fovea or the cells in the brain

The difference between the images does not assume any importance until fusion into a conscious picture in the brain occurs Simultaneous binocular vi sion is also essential for the diagnosis and measurement of aniseikonia The apparatus which Ames and his co workers constructed for the measurement was dependent on binocular vision In the standard eikonometer the relative differences between the images are measured as a percentage With the space eikonometer the altered spatial perception which is present in aniseikonia is measured It is averaged and measured as a percentage by means of magni fying lenses *A Ames* (1945) and *H Burian & K Ogle* (1945) found good cor relation of the results obtained by the two eikonometers The images of dif ferent size or form are thus directly related to the subjective change in spatial perception This is usually not noticed in the everyday environment It appears in a situation lacking in factors aiding monocular depth perception

An attempt has been made to find the incidence degree and clinical im portance of aniseikonia No population study has been made On the contrary

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than the skiascopic value Astigmatism of up to 2 dioptres has been fully corrected Higher astigmatism has been under corrected initially In some cases smaller changes in the spectacle corrections have been made during the period of treatment as indicated by the visual acuity and the corneal astigmatism as measured by the ophthalmometer In addition to this treatment some of the material (Group B) has been given an all over iseikonic correction of 0 75 1.25 % per dioptre of anisometropia. The cases have been assessed about 0 5 1 2 and 3 years after the beginning of treatment

Material

As previously mentioned in the Introduction the material was composed of 18 % of 4 year olds from each of several year groups from the same geographical area It has been collected through sight testing *W Nordlow & S Joachimsson* (1966) and is representative of the Swedish population Of these 4 year olds those with anisometropia of 2 dioptres or more have been made the subject of this study Anisometropia of this degree occurs in 0 72 ± 0 155 % of 4 year olds The degree of anisometropia is defined as the difference between the two most hypermetropic principle meridians in hypermetropia or the two least myopic principle meridians of both eyes in myopia At astigmatism of unequal degree the difference in the other principle meridians is another The material can be divided into two groups with respect to treatment

A Correction with conventional lenses and

B Even magnifying correction iseikonic lenses

Group A comprises in addition to the anisometropes which were described in 1966 *W Nordlow & S Joachimsson* and were born between 1953 and 1956 inclusive also those born between 1957 and 1959 inclusive thus in all seven year groups They include a total of 37 cases From these were removed two who had moved away from the area one who failed to attend and two who received iseikonic correction during the period of treatment These five cases did not differ from the remainder concerning the results of the initial examination Thus there remain 32 cases in this group

In Group B are those anisometropes born between 1960 and 1962 inclusive thus from three year groups The group consists of 15 cases

As has been mentioned the sight testing was performed during the fourth year of life Because of some delay in examination and refraction in the eye reception the spectacle correction has been delayed Some have reached the age of five years (Table 1)

The refractive errors are shown in Table 2 In group A the anisometropia varied between 2 and 7 dioptres. Uncomplicated anisometropia, the same dif

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From the Departments of Ophthalmology and Diagnostic Roentgenology
University Hospital Lund Sweden

CAROTID CAVERNOUS FISTULA WITH CONTRALATERAL EXOPHTHALMOS

BY

H G BYNKE and H O EFSING

A fistula between the internal carotid artery and the cavernous sinus is usually caused by trauma but may result from spontaneous rupture of an aneurysm as a rule an arteriosclerotic one Irrespective of the pathogenesis arterial blood *will be shunted in retrograde direction from the cavernous sinus into the su*perior ophthalmic vein This results in exophthalmos which may be pulsating and in engorgement of superficial and retinal veins Other symptoms such as frontal pain pulse synchronous noises in the head and palsies of ocular muscles may occur

Usually the exophthalmos appears on the side of the fistula but simultaneous or subsequent involvement of the opposite orbit is common due to the presence of connections between the cavernous sinuses on both sides

The exophthalmos may be mainly or exclusively contralateral This is a rare finding as demonstrated by the fact that in reports on this phenomenon each author has presented only one case of his own *In this paper the literature will* be reviewed and a new case in which the mechanisms were elucidated by caro*tid angiography will be reported*

Review of the literature

The literature contains detailed reports on 13 cases of carotid cavernous fistula with mainly contralateral exophthalmos The principal data are collected in Table 1

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In 30 % of the cases agreement is good in 40 % less good and in 30 % there is no aniseikonia according to Ogle (cit *Davis* 1959) *R J Davis* (1959) considers that with pre school children it is better to treat with an estimated aniseikonic correction than with none at all Bannon suggests approximately 1 % and Ogle 1 5 % magnifying for each dioptre of anisometropia Davis believes that at present it is best to correct the total meridional error irrespective of the position of the axes There does not appear to be a published study of the results of applying the estimated iseikonic correction in anisometropia in pre school children

Method

The visual acuity has been measured at the screening examination and in more detail in the Eye Department with Bostrom Marques Squares according to the method of *W Nordlow & S Joachimsson* (1962) The angular visual acuity is measured The visual acuity has been recorded as the smallest square the opening of which has been given correctly four times in succession This value has been used to compare the results of examinations on different occasions

To obtain an idea of how the visual acuity as measured above agrees with the method using letters in rows according to Monoyer both methods have been used when the children have reached the age of 8 years With the latter method recognition and ability to seperate are both involved It was found that of 350 consecutively tested eyes with refractive errors and reduced visual acuity which improved on treatment to 5/5 294 had visual acuity 1 0 49 had 0 9 5 had 0 8 and 2 had 0 7 If allowance is made for the error of the method in comparing the two methods at ± 0 1 98 % show complete agreement

The refraction was determined by skiascopy (stigmatoscopy) after atropinisation for 3 days (1 % Atropine Sulphate solution twice daily) A point source of light has been used the light from which has been projected into the eye with a plane parallel glass The examinationdistance has been 0 5 metres The relation between the skiascopic value and the optical condition of the eye in accommodative rest has been calculated previously *W Nordlow* (1949)

The fixation of the worse eye has been assessed in some cases by means of the visuscope

Binocular function has been assessed on the synoptophore The balance has been assessed using the spider and net for the fusion amplitude L and F (8 × 6 mm) have been used and for stereopsis photocopies of Zeiss test objects with silhouettes for the Zeiss stereoscope Examination of stereoscopic vision has been confined to the preliminary test and picture 5

The whole material has been given spectacle correction of 0 5 dioptres less

Table 1
Clinical data of 13 cases of carotid cavernous fistula with contralateral exophthalmos

Author(s)	Sex Age	Origin	A Ipsilateral ocular signs	B Contralateral ocular signs (in add to exophthalmos)	Interval between A and B	Carotid compression test	Angiography
Reif (1899)	f 25	traumatic	palpable pulsation paresis N III and VI	palpable pulsation papilloedema	0	+	no
Pincus (1907)	m 31	traumatic	optic atrophy paresis N III IV and VI	palpable pulsation paresis N VI	7 weeks	+	no
Dandy & Follis (1941)	m 53	traumatic	exophthalmos optic atrophy paresis N III and VI	visible pulsation optic atrophy paresis N VI	0	+	no
Ramos & Mount (1953)	f 54	traumatic	none	ptosis paresis N VI		—	yes
Tamler (1954)	m 86	spontaneous	paresis N III and VI	paresis N III and VI	2 months	+	yes
Graeleau & Namin (1954)	f 67	spontaneous	none	papilloedema retinal haemorrhages paresis N III		?	yes
Kunc & Dulik (1954)	m 31	traumatic	none	visible pulsation paresis N VI		+	yes
Rouvès & Rouves (1955)	m 21	traumatic	none	total ophthalmoplegia		+	no

Table ?

The refractions of 47 anisometropes at the start of treatment

Group	No Cases	No Eye Worst	No Eye Best	Refraction H	Refraction H Ast	Refraction M	Refraction M Ast	Refraction An	Refraction An Ast	Anisometropia in dioptres 2–	2.5–	3–	3.5–	4–	5–	6–	*Case* difference in astigmatism between right and left eye / *Eye* degree of astigmatism in dioptres 0–	0.5–	1–	1.5–	2–	2.5–	3–	3.5–
A	3?							1?	20	16	?	?	3	4	2	3	3	7	3	2	3	1		1
		3		10	19	2	1											9	4	1	3		1	2
			32	25	6	1												5	1					
B	15						2	6	7	4	1	3	?	2	2	1		4	4	1				
		15		6	7		2											3	2	2	2			
			15	1?	1		2											1	?					

Walsh (1957)	m 48	traumatic?	paresis N VI	corneal hypaesthesia paresis N III and VI	0	+	?
White et al (1955)	f 49	traumatic?	none	visible pulsation paresis N III and VI		+	yes
David et al (1964)	m 24	traumatic	optic atrophy	papilloedema	8 months	+	yes
Girard et al (1966)	m 45	traumatic	paresis N VI	external ophthalmoplegia	2 weeks	+	yes
Graham (1966)	f 64	traumatic	paresis N VI	visible pulsation paresis N VI	A 9 months after B	+	yes

Table 1

Age distribution of 47 anisometropes at the beginning of treatment

Group	No of cases	Age in years when corrected							
		With conventional lenses				Also with iseikonic lenses			
		4–4 5	4 5–5	5–5 5	5 5–6	4–4 5	4 5–5	5–5 5	5 5–6
A	32	5	21	5	1	–	–	–	–
B	15	2	7	5	1	2	6	5	2

ference between all meridians in both eyes occurred in 12 cases In the other 20 cases there was also astigmatism with a difference of 0 3 5 dioptres between both eyes In 18 of 32 cases the anisometropia was between 2 and 3 dioptres and in 10 of 20 cases the astigmatic difference was less than 1 dioptre The refractive errors in Group B did not differ from those in Group A

With iseikonic correction of astigmatism with oblique axes there is a so called declination error as has been referred to in the review of the literature It is therefore of interest in this connection to see how frequently oblique axes occur *in a representative group of anisometropes (A and B) A deviation* greater than $\pm$ 10° from vertical or horizontal axis occurred in 8 cases out of 29 of the worst eyes and in no cases out of nine of the best eyes

Results

Group A (32 cases) With regard to the change of anisometropia it may be mentioned that it remained unchanged during the period of observation in 15 cases It reduced by 0 5 1 5 dioptres in 15 cases 2 5 diopters in one case and increased in one case In only three cases the anisometropia reduce to less than 2 0 dioptres

The visual acuity could be measured at the first examination *in 31* cases and varied in the worst eye from 5/15 to 1/50 without correction After 3 years of correction with conventional lenses it had improved to a greater or lesser extent in all cases (Table 3) A good visual acuity 5/5 and 5/6 was achieved in 12 eyes In explanation it can be proposed that only a slight or absent induced aniseikonia was present In 10 eyes a visual acuity of 5/10 and in 10 eyes 5/15 5/30 was achieved *thus poor results One can say that 1/3 of the cases responds*

It should be added that one case was reported by Velpeau as early as 1839 as briefly mentioned by *Pincus* (1907) *Schirmer* (1898) described another case that seems to have been identical to that of *Reif* (1899) *Jefferson* (1950) reported on one case in an unpublished lecture Furthermore one case was briefly mentioned by Taveras & Wood in their textbook of Diagnostic Neuroradiology

Bilateral ocular changes were present in 8 of the 13 cases In 7 the contralateral exophthalmos appeared simultaneously with the ipsilateral changes or after an interval of two weeks to three months but in the case of *Graham* (1966) the ipsilateral sixth nerve paresis appeared later than the contralateral exophthalmos In the case of *Dandy & Follis* (1941) the ipsilateral exophthalmos had disappeared after several years and the clinical picture was dominated by the contralateral exophthalmos Exclusively contralateral changes existed in 5 cases Visible or palpable pulsation of the bulb was noted in 6 cases

The patient often describes pulse synchronous noises in the head which can readily be heard with a stethoscope The bruit may be eliminated by compression of the carotid artery in the neck on the same side as the fistula but not by compression on the other side This examination often incorrectly called Matas test was positive in at least 11 of the 13 cases Only in the case of *Ramos & Mount* (1953) was the test negative due to the fact that the fistula was largely supplied by the vertebral arteries

A prerequisite for the development of ipsilateral exophthalmos is a free communication between the cavernous sinus and the superior ophthalmic vein The cause of a blockage is proposed by *Reif* (1899) to be a thrombosis of the superior ophthalmic vein In the case of *Dandy & Follis* (1941) an occlusion of the ipsilateral vein was verified at autopsy In the case of *Tamler* (1954) also examined at autopsy no ophthalmic vein could be found entering the cavernous sinus *Ramos & Mount* (1953) and several subsequent authors found no communication between the ipsilateral superior ophthalmic vein and the cavernous sinus at angiography *Tamler* (1954) suggested that this lack of communication might be due to one of several conditions e g a thrombus or a traumatic rupture of the vein an obstruction of its proximal portion by a dilated carotid artery or an anomaly of its course

Case report

A D a man aged 74 had previously been treated for myocardial infarction

One night he woke up with an intense frontal headache Three hours later it had diminished but not disappeared In the morning he also complained of double vision

Two days later he was examined by an ophthalmologist who found paresis of the medial rectus the palpebral levator and the pupillary sphincter of the left eye, but no other signs

Table 4

Type of fixation in 19 of 32 anisometropes who had correction with conventional lenses for 3 years (Group A)

Worst eye		Type of fix	Final visual acuity					
Examined	No		5/5	5/6	5/10	5/15	5/20	5/30
Yes	15	f		4	10	1		
Yes	4	pf				3	1	
No	13		3	5		3	1	1
Total	32		3	9	10	7	2	1

f = foveolar
pf = para foveolar

(P $<$ 0 001) A half year visual acuity of 5/15 or less indicates a poorer response to treatment with conventional lenses

Group B (15 cases) The anisometropia remained unchanged during the period of observation in 7 cases reduced by 0 5 1 5 dioptres in 6 cases and increased 1 2 dioptres in 2 cases A reduction to less than 2 dioptres occurred in one case The agreement with Group A is good

As in Group A the visual acuity was 5/15 1/50 in the worse eye at the first examination After using iseikonic correction in 12 cases for 3 years and in 3 cases for 2 years the visual acuity was 5/5 in 6 cases and 5/6 in another 6 cases i e good in 12 cases In 2 cases the visual acuity became 5/10 and in one eye 5/30 (Table 5) Thus poor visual acuity occurred in one case out of 15 against 10 cases out of 32 in Group A On testing with the χ^2 test it was revealed that a visual acuity of 5/5 and 5/6 was obtained significantly more often with iseikonic lenses than without (P $<$ 0 01)

With regard to the type of fixation in the worse eye at the first examination in Group B of 14 cases examined 12 had foveolar fixation and 2 parafoveal fixation At the final examination one of the 14 cases still had parafoveal fixation (visual acuity 5/30) The child whose fixation had not been tested at the first examination had foveolar fixation at the final examination Parafoveolar fixation was thus present in one case out of 15 corrected with iseikonic lenses against 5 cases (4 definite) out of 32 without such correction

Binocular vision was examined in 14 cases Of these 13 had N R C and fusion amplitude The fourteenth case had parafoveal fixation and suppression. With regard to stereopsis 13 cases managed the preliminary test and 7 cases picture 5 also As it was the first time the children had performed this test the result may be regarded as a minimum value From examination of adults with

The next day the ptosis and the mydriasis had increased The patient was referred to the Department of Internal Medicine at the local hospital where he was treated as an in patient. The headache was of moderate intensity and located around the left eye. General and neurological examinations were negative except for the ocular findings. The blood pressure was 170/95 Bilateral carotid angiography one week after the appearance of the symptoms disclosed a carotid cavernous fistula on the left side and a retrograde filling of the superior ophthalmic vein on the right side

The following day the patient noticed a swelling of his right eye At ocular examinations the eye lids and conjunctiva of the *right eye* were found to be swollen and the conjunctival and retinal veins engorged and there was a right sided exophthalmos of 9 mm No pulsations of the bulb were observed but a pulse synchronous bruit was heard over the temporal regions The left oculomotor paresis was unchanged Later the corrected visual acuity of the right eye was found to decrease successively from almost normal to 0 4

Due to this progressive course he was taken into the Department of Neurosurgery University Hospital Lund During his stay in this hospital the intensity of the headache varied and he was sometimes disturbed by a noise in his head General and neurological examinations were still normal except for the ocular findings

Ocular findings

Visual acuity finger counting 1 meter R E 0 7 L E
Perimetry concentric contraction right field Normal left field
Ocular tension normal both eyes
Hertel 25 mm R E. 15 mm L E
R E. non pulsating exophthalmos Total ptosis external and internal ophthalmoplegia Hyperaemia and oedema of eye lids and conjunctiva Corneal hypaesthesia. Keratitis with oedema and epithelial defects Slight papilloedema and dilated retinal veins
L. E. slight ptosis and paresis of the medial rectus Normal pupil Senile degeneration of the macula

A pulse synchronous bruit was heard over both frontal and temporal regions It ceased at compression of the left common carotid artery but not of the right

Bilateral carotid angiography

The carotid arteries and their branches were tortuous and widened and multiple arteriosclerotic irregularities were present. As in the previous examination there was a shunting of blood from the left carotid artery to the cavernous sinus and to the right superior ophthalmic vein. The width of the latter vessel had increased There was still no filling of the left superior ophthalmic vein. (Figs. 1a c)

During the week following the angiographic examination the headache and the bruit disappeared and the exophthalmos began to decrease Due to this spontaneous improvement no operation was performed and he was discharged to his local hospital Later there was regression of the keratitis and improvement in vision. Six months after the onset of his illness the visual acuity of the right eye was 0.5 and the exophthalmos was only 1 5 mm The cornea was normal There was still a slight paresis of the right medial rectus muscle

A month later the patient had acute abdominal pain, caused by an aneurysm of the

Table 3

Improvement of vision in 32 anisometropes who had full correction with conventional lenses for 3 years (Group A)

Observ time in years	No of eyes			Visual acuity							
	Not Examined	Examined									
		Worst	Best	5/5	5/6	5/10	5/15	5/20	5/30	5/50	4 1/50
0	1	31*					4	6	8	5	8
0 5	4	28			5	6	8	4	4		1
1	0	32			7	11	4	5	4	1	
2	2	30		3	7	13	5		2		
3	0	32		3	9	10	7	2	1		
0	1		31*	17	7	6	1				
0 5	4		28	20	7	1					
1	1		31	27	4						
2	2		30	27	3						
3	0		32	31	1						

* Without correction lens

well to the treatment and that an induced aniseikonia may have prevented the development of full visual acuity in the remaining 2/3 The type of fixation was examined in 19 cases (Table 4) It was found that 4 cases lacked foveolar fixation It was suspected that a further 4 cases belonged to this group which thus represents a quater of the total It may be considered as an unexpectedly high frequency to ascribe to the aniseikonia

It would of course be valuable if it could be decided at the beginning of treatment which cases would have poor visual acuity and then start with isei konic lenses After scrutiny of the initial visual acuity the degree of anisome tropia and astigmatism in correlation with the final visual acuity and testing with the χ test no guidance is obtained concerning the importance of these factors On the contrary it shows that the visual acuity obtained after the wearing of a spectacle correction for half a year is a more certain parameter for assessing the prognosis It is of course a test of the response of the eye Of 19 eyes with a half year visual acuity of 5/15 or less 3 obtained a visual acuity of 5/6 or better and 16 a visual acuity of 5/10 5/30 Of 13 eyes with a half year visual acuity of 5/10 or better 11 achieved a visual acuity of 5/5 or 5/6 and 2 a visual acuity of 5/10 The χ^2 test shows that the difference is significant



1a



1b



1c

Figs 1a c
Left sided carotid angiography showing a left sided carotid cavernous fistula and a filling of the superior ophthalmic vein on the right side but not on the left

abdominal aorta This was treated surgically but six days after the operation he suddenly died from a second myocardial infarction At post mortem the cavernous portion of the left internal carotid artery was found to be dilated and there was an advanced arteriosclerosis of the basal cerebral vessels The orbital vessels were not examined

Comments

In the reported case the carotid cavernous fistula was of the so called spontaneous type It occurred in an old man who was subject to several arterio

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With regard to the type of fixation in the worse eye at the first examination in Group B of 14 cases examined 12 had foveolar fixation and 2 parafoveal fixation At the final examination one of the 14 cases still had parafoveal fixation (visual acuity 5/30) The child whose fixation had not been tested at the first examination had foveolar fixation at the final examination Parafoveolar fixation was thus present in one case out of 15 corrected with iseikonic lenses against 8 cases (4 definite) out of 32 without such correction

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sclerotic diseases and who ultimately died from myocardial infarction following an operation for an aortic aneurysm

The initial ocular signs were slight and located to the side of the fistula After one week they were accompanied by a pronounced contralateral exophthalmos In combination with trigeminal involvement this resulted in a keratitis with visual deterioration Eight weeks after the onset of symptoms a spontaneous regression of the ocular changes started

As in almost all the other similar cases reported by previous authors the carotid compression test was positive and found to be valuable for the determination of the side location of the fistula

The absence of ipsilateral exophthalmos is in accordance with the angiographic finding of no communication between the cavernous sinus and the superior ophthalmic vein on that side This is in agreement with the observation of *Dandy & Follis* (1941) *Ramos & Mount* (1953) *Tamler* (1954) and other previous authors In our opinion the most probable explanation is that there was a thrombosis in the superior ophthalmic vein In our case a lack of communication due to vascular abnormalities seems unlikely

Summary

Cases of carotid cavernous fistula with mainly or exclusively contralateral exophthalmos are rare This paper contains a review of the literature concerning these cases and a report on another case

The exophthalmos is caused by an engorgement of the orbital veins The absence of ipsilateral exophthalmos in our case and in most of the previously reported cases was probably due to a thrombosis in the superior ophthalmic vein blocking the passage to the veins in the orbit

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technique and embedding technique the tissue preservation obtained in this material was not of a quality permitting a more precise analysis however

In superficial dendritic keratitis the lesion are generally well defined and well demarkated As judged from examination in the slit lamp microscope the remaining areas of the corneal epithelium look undamaged at least at early stages of the disease One thus gets the impression that the infection is restricted to the lesions The present electron microscopic investigation was undertaken in order to establish whether or not signs of infection with virus could be found in the cells of the clinically undamaged areas of the corneal epithelium It appears that the results of such a study would be of interest as to the therapeutical measures in dendritic keratitis as well as to the question of recurrence of the disease

Materials and Methods

Two young men both having a history of dendritic keratitis four and six years ago respectively were examined two days after the onset of symptoms of the first recurrence Upon examination in the slit lamp microscope lesions typical of dendritic keratitis stained with fluorescein were seen in the corneal epithelium. In one of the cases herpes simplex virus was also identified by means of isolation and serological tests Strips of clinically undamaged corneal epithelium located two to five mm away from the closest lesion were carefully removed from the cornea under visual control in the slit lamp microscope A spud designed for removal of corneal foreign bodies was used for the dissection Strips containing a lesion were also removed All strips were immediately immersed into cold 1% osmium tetroxide fixative buffered with Veronal acetate and made approximately isotonic with plasma After dehydration in acetone the tissue was embedded in Vestopal W The sections subsequently stained with uranyl acetate and lead citrate were examined in a Siemens Elmiscop I which was kindly put at my disposal by prof B Thorell Department of Pathology Karolinska Sjukhuset Stockholm

Results

The cells of the necrotic tissue lining the active dendritic lesions contained large numbers of virus particles morphologically identical with herpes simplex virus This finding was expected and will not be dealt with in detail here

All micrographs of the present investigation were taken of clinically intact

corneal epithelium located two to five mm away from the closest visible lesion A survey picture of some cells from one of these biopsies is shown in Fig 1 At this magnification the cells appear normal At somewhat higher magnification intranuclearly located structures with an appearance similar to herpes simplex virus could be found in the great majority of the cells investigated however (Figs 2 and 4) The number of virus particles per cell was fairly small compared to that of the cells lining the lesions The virus particles were often located close to electron dense areas in the nucleoplasm

An intranuclearly located virus particle (or virion) consisted of an inner core and an outer capsid (Figs 3 and 5) The core which is the DNA containing part of the virus particle was generally spherical or slightly oval Its center was in most cases less opaque than its periphery This was evident particularly



Fig 1

Survey picture of superficially located cells of human corneal epithelium This micrograph as well as the following micrographs were taken of clinically intact corneal epithelium located two to five mm away from the closest visible lesion in dendritic keratitis × 3,00

Graham M V Arterio venous shunt in the cavernous sinus with contralateral ocular signs Brit J Ophth *50* (1966) 599 602
Kunc Z & F Dulik Carotid cavernous aneurysm with contralateral pulsating exophthalmos Čsl Ofthal *10* (1954) 30 36
Pincus F Spontanheilung eines traumatischen pulsierenden Exophthalmus Ztschr f Augenheilk *18* (1907) 33 41
Ramos M & L A Mount Carotid cavernous fistula with signs on contralateral side. J Neurosurg *10* (1953) 178 182
Reif E Ein Fall von doppelseitigem hauptsachlich gekreuztem pulsierendem Exophthalmus Beitr z Augenheilk *4* (1899) 545 562
Rouves L & C Rouves Etude E E G d un cas d anevrysme carotido caverneux post traumatique a symptomatologie oculaire contro laterale Rév neurol *93* (1955) 486-493
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Taveras J M & E H Wood Diagnostic Neuroradiology Baltimore Williams & Wilkins Co (1964) 1960 pp
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White J C Love J G & N P Goldstein Carotid cavernous fistula on left side with ocular symptoms on right side Proc Staff Meet Mayo Clin *33* (1958) 441 445

prisms was rotated 90°, in order to present an image rotated 180° to one of the eyes (Fig 2 and 3) The displaced part of the square wave gives the transverse disparity necessary for the perception of stereopsis and the observer just has to determine whether the middle segment of the target is situated in front of the reference lines or behind them It must be observed that with this method of producing a stereo situation the pupillary distance is of no importance

The two disparate images so produced are easily "fused" by most observers with normal bifoveolar fixation The sum of the vernier off sets – the stereo disparity – must of course be within the limits of Panum s zone and the test object on the oscilloscope screen must be symmetric with regard to a vertical plane in the center of the target

By means of this prismatic device any type of heterophoria of the observer s

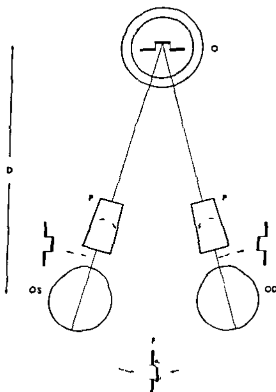


Fig 3

Schematic illustration of the method by which a stereoscopic situation is produced By means of a prismatic device (P) the images of the square wave on the oscilloscope (O) are rotated clock wise for the left eye and counter clock wise for the right eye When the images are fused a transverse disparity is produced The displaced segment of the target is perceived either in front of or behind the plane of the reference lines depending on the direction of the displacement (a)

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From the Department of Experimental Ophthalmology
University Eye Clinic Lund Sweden

OBSERVATIONS ON VERNIER AND STEREO ACUITY WITH SPECIAL REFERENCE TO THEIR RELATIONSHIP

BY

GÖRAN STIGMAR

Introduction

The vernier and stereo visual functions are in many respects very closely connected as noted by many authors (*Links* 1952 *Ludvigh* 1953 *Le Grand* 1956 and others) Both are said to be based on the perception of relative direction differences (*Ludvigh* 1953)

Vernier acuity (nonius acuity or aligning power) is the ability to detect a break in a contour or irregularity in a line As pointed out by *Ludvigh & Bair* (1953) a distinction must be made between the perception of relative direction differences in a vernier or a stereoscopic situation and the perception of the absolute location of an object in space a fact which makes the traditional terms direction (or localization) sense of the eye inappropriate names for this capacity of the visual system

Stereoscopic vision is in this investigation only studied within the limited range of binocular vision which *Ogle* (1952) has defined as the region of patent stereopsis The stereoscopic acuity in this range has an accuracy comparable with the vernier acuity

It has been almost generally accepted that the disparity (transverse disparity) between the retinal images is the only stimulus necessary to release the perception of stereopsis. This conception was stressed not least by *Ogle* (1959)

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eyes can be compensated This can be accomplished by changing the position of the axes of the prisms With two micrometer screws the prism axes are most carefully adjusted with regard to the optic axes of the eyes

(d) Monocular and binocular vernier functions

From experiences with the stereo vernier situation it seemed logical to study also the monocular versus the binocular vernier function

The examination of monocular and binocular vernier performances was car ried out in principally the same way as previously described In a random way the subject had to interpret a vernier pattern (target Type A) with its different separation distances monocularly or binocularly In order not to produce a change of the size of the pupil in the monocular situation by occluding the contralateral eye a diffusing filter was placed in front of that eye Three ex perienced subjects took part in the examination

(e) Experimental arrangements

Throughout the various experiments all parts of the arrangement were kept constant. The illumination of the room (of about 15 lux) the luminance of the test object and the background illumination on the oscilloscope screen were chosen to give optimal viewing comfort and visual acuity In some of the experiments a background target consisting of concentric circles was used as a stimulus for fusion During the course of the experiments however it turned out to be unnecessary to use this fusion stimulating background since all the experiments were made in an orthophoric state of binocular vision It was found that the reference lines (r) alone were a stimulus for fusion strong enough to maintain a stable bifoveolar vision throughout the examination session.

It is known from earlier experiments (*Baker* 1949 *Foley Fisher* 1968) that vernier acuity is dependent on the wave length of illumination In this in vestigation the background on the oscilloscope was pale yellowish green and the test object itself had a radiant energy distribution with its maximum in the middle of the visible spectrum (5100 Å)

The subject was placed 5 m in front of the test object viewing the target through the prismatic device Uniformly illuminated unstructured screens with small apertures restricted the binocular field allowing nothing else but a field subtending 8 around the test object to be seen by the observer Due to the rotating effect of the prisms it was necessary to have a neutral surrounding visual field

Each experimental session consisted of a stereo vernier block of 10 min (Fig 4) 5 min for each situation starting with one of the targets presented either in the vernier or stereo situation in a random way The maximum expo

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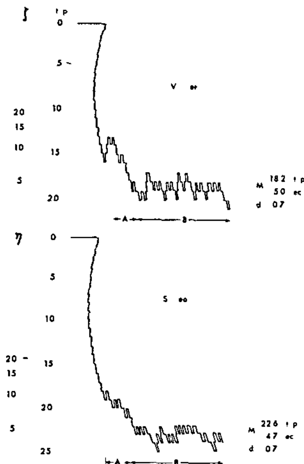


Fig 4

A stereo vernier block as it appears from the recorded graphs A illustrates the adjustment period and B the 4 minute period which is the base for the mean value calculations In the illustrated recordings there are no significant differences between vernier and stereo thresholds

sure time for each interpretation was 4 sec with short intervals of 0 5 sec Most observers made use of only about 2 sec of exposure time thus having time for about 150 trials during a 5 minute period (right or left in front of or behind) Each block was followed by a pause No subjects was required to have more than three sessions in any one day

Definitions

Most of the symbols are indicated in Fig 1 4 The off set of the oscilloscope line is designated *a* which gives a retinal displacement *a'* If the observation

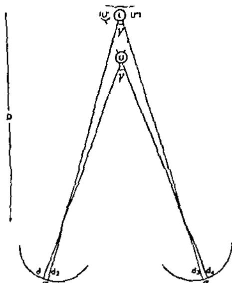


Fig 1

Two dimensional illustration of a stereo vernier situation as seen from above modified after Walls The test object consists of two rods (L and U) vertically arranged In the vernier situation the upper rod is either to the right or to the left of the lower rod and the dislocation (a) between them gives rise to the different visual directions (d_1 d_4) with a displacement (a) in each eye If the upper rod is placed in front of (or behind) the lower rod in the intersection of d_1 and d_4 and the resulting transverse disparity (?a) is small a stereoscopic situation is given with the same monocular disparity In this investigation a *vertically arranged three rod test* was used as a target and the change from the vernier situation to the stereoscopic one was accomplished by a pris matic device giving an identical test situation for the testing of both acuities. The

$$\text{angle of disparity } (\eta) = \gamma - \gamma \;= \frac{2a}{D}$$

that the stereo acuity was not as much affected as the vernier acuity when the separation distance was increased Berry concluded the stereoscopic thresholds were for the most part too low to be accounted for by a simple summation of the two separate monocular vernier components Thus he found stereoscopic thresholds between ? 4 sec and vernier thresholds between 3 7 sec in three sub jects within a certain range of separation differences between the rods

Method

With a *new automatic technique* described by *Arakau* (1967a) using a square wave on an oscilloscope as the same test object for both the vernier and the

distance is D (from the nodal point of the eye to the fixation point) the angle subtending the off set is $\frac{a}{D}$ (radians)

In the vernier situation the retinal displacements (a) in both eyes have the same direction and the vernier off set is defined by $\zeta = \frac{a}{D}$ In the stereo situation the retinal displacements are in opposite directions and the angular disparity of the two off sets then will be $\eta = \frac{2a}{D}$ The thresholds of vernier and stereoscopic perception ζ_t and η_t are obtained from the recorded graphs (Fig 4) and they are expressed in terms of $\frac{a_t}{D}$ and $\frac{2a_{st}}{D}$ where a_t denotes the threshold vernier off set and $2a_{st}$ the threshold stereo disparity As statistical quantities they will be discussed in the following section

Material

(a) Observers

Five experienced observers served as subjects Their corrected visual acuities according to Monoyer s letter chart were 1 0 or more on both eyes Refraction varied from + 0 5 to − 2 0 In order to eliminate the training effect – which is a striking fact in vernier acuity as well as in stereoscopic acuity – the subjects were previously trained in several sessions Then the observers had reproducible threshold values for both functions

(b) Evaluation of the records

Every experimental examination started with the test object on "step 0 where the vernier off set was 2 mm ($\frac{a_0}{D}$ = 83 sec arc) After three correct interpretations the test object corresponding to step 1 was presented ($a_1 = \frac{a}{1\ 2^1}$) and in the same way the following steps were automatically presented for interpretation by the subject Thus a step curve was recorded indicating the number of transitions from one step to another during a 5 minute period

Two parts of each curve can be identified The first one – the adjustment period – lasts about one minute during which the subject approaches the steady level which is typical for the second period

Only the second period of about 4 minutes was used for calculations and only those curves where no clear trend towards improvement or deterioration

With the investigations by *Julesz* (1960 1963 1964) and others it has become clear that stereopsis cannot always be defined in terms of retinal disparity According to *Lawson & Gulick* (1967) there are reasons to extend the concept of disparity to include not only the retinal disparities but also those induced on a higher visual level In their experimental work however, the same authors conclude that irrespectively of where the disparity is induced stereopsis can be handled by the classical model of stereopsis

For the purpose of this paper these questions concerning the physiological processes behind the nature of stereopsis are of secondary importance If the patterns used as stimuli for the stereo perception are simplified then it is the relative visual directions which are of importance for the information available to higher visual centers – a fact justifying the classical geometrical approach to stereopsis

Using different test objects and experimental arrangements many investigators (for ref see *Hirsch & Weymouth* 1948 *Foley-Fisher* 1968) have shown that the limiting values of the vernier and the stereo acuities are of about the same order of magnitude (about 2-10 sec arc in the nodal point of the eye) It has also been shown that the two functions are equally influenced by changes in the luminance of the test object (*Leibowitz* 1955)

Although considerable information is available concerning vernier and stereo acuity as two separate visual functions few systematic studies have been carried out on the relation between them

The aim of this investigation has been to study the vernier and stereo functions from a quantitative point of view with a stimulus pattern which is supposed to give the same amount of information in the vernier and stereo situation respectively

As *Ogle* (1962) emphasized it is essential in such a comparative study to use equivalent methods in testing the two functions

The Stereo Vernier Situation

The main purpose in this investigation has been to obtain an experimental situation free from secondary cues which might influence the results such as relative size of the targets interposition movement parallax or convergence

As suggested by *Walls* (1943) a stereo vernier target (Fig 1) is the adequate test object to use in an experimental investigation with the purpose of determining the relations between these two visual functions Stimulated by the theoretical considerations of *Walls Berry* (1948) took up the ideas of a stereo vernier test object With a target consisting of two cylindrical rods one above the other he studied the vernier and stereo acuities under similar conditions By changing the separation distance between the rods he was able to show that the two functions were not equally influenced by this procedure Thus he found

can be identified The criteria for excluding such curves have been a difference exceeding 5 steps between the first and last step of the second period

The size of the easiest step (a_0) is so chosen that it is always correctly interpreted whereas the smallest steps are so difficult that they are only guessed To an object a_n we can adjoin a probability of correct interpretation, p_n which goes from 1 to 0 with increasing difficulty (if allowance has been made for the chance of correct guessing) During the course of testing a number of transitions are made on a set of objects $\{a_n\}$ (Fig 4) It is possible to estimate the probabilities connected with the objects from the numbers of these transitions

The whole set of probabilities $\{p_n\}$ has not been determined at each testing period for practical reasons It can be shown (*Krakau* 1967a) that the probability of the step corresponding to the mode of distribution being perceived is ≥ 0.6

Since the distribution of transitions in the second period can be considered as symmetrical around a mean value it has been convenient to characterize the distribution by the arithmetic mean (M) and the standard deviation (s d) This mean value has arbitrarily been denoted "the threshold value"

In order to reduce the effect of temporary fluctuations of the level of performance each of the experimental sessions has been repeated on another independent occasion The results presented in the following section are the averaged values

Results

(a) Obtained with target Type A

The individual results are given in Table I for each of the five different separation distances between the reference lines and the dislocated part of the line

The mean values of the five subjects are given as a graph (Fig 5) where the ordinate indicates the threshold values and the abscissa the separation distances

(b) Obtained with target Type B

The test object of Type B can be regarded as one of Type A with the separation distances b = 0 The results are presented as those for Type A (Table II and Fig 6 respectively)

(c) Binocular vernier performance versus monocular performances

The results are presented in Table III and in a graph (Fig 7) Target Type A with the same separation distances as earlier described has been used as test object

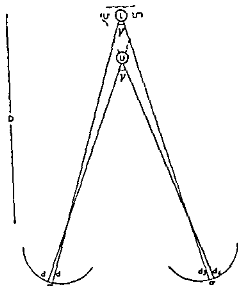


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$$\text{angle of disparity } (\eta) = \gamma - \gamma' = \frac{2a}{D}$$

that the stereo acuity was not as much affected as the vernier acuity when the separation distance was increased Berry concluded the stereoscopic thresholds were for the most part too low to be accounted for by a simple summation of the two separate monocular vernier components Thus he found stereoscopic thresholds between 2 4 sec and vernier thresholds between 3 7 sec in three subjects within a certain range of separation differences between the rods

Method

With a new automatic technique described by *Krakau* (1967a) using a square wave on an oscilloscope as the same test object for both the vernier and the

Table I

Vernier and stereo thresholds related to the separation distance (Type A)

Extension of the target (*min arc*)	14		18		24		34		50	
b (min arc)	2		4		7		12		20	
Subject	ζ_t	η_t	ζ_t	η_t	ζ_t	η_t	ζ_t	η_t	ζ_t	η_t
G L.	4.6	37.2	7.4	13.9	10.6	9.1	12.6	14.5	17.8	17.5
G S	4.9	23.0	5.0	10.1	7.2	7.5	11.8	14.5	15.1	18.7
V W	2.4	21.0	3.9	8.0	7.4	10.6	7.4	11.6	15.7	14.2
I B	4.6	16.9	7.7	6.5	12.4	7.5	11.8	10.6	16.2	16.3
O W	5.3	16.6	7.1	7.7	10.8	9.5	13.3	12.8	17.5	14.8
M (n = 5)	4.4	22.9	6.9	9.2	9.7	8.8	11.4	12.8	16.5	16.3
s.d.	1.1	8.4	1.7	2.9	2.3	1.3	2.3	1.7	1.2	1.9

The vernier (ζ_t) and stereo (η_t) thresholds are expressed in sec arc

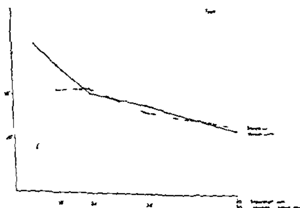


Fig 5

Curves relating the thresholds (in sec arc) of the vernier and the stereo functions to the vertical separations (b) and the extension (e) target Type A. Average values for 5 individuals

(d) Precision of the results

An examination of the individual step curve will reveal fluctuations of the

stereo performances it has been possible to study the vernier and stereo acuities during identical situations and to make the comparison of the results on the bases of graphically recorded acuity determinations

(a) The Apparatus

A full description of the apparatus will be found elsewhere (*Krakau* 1967a) and only some of the arrangements which are essential or original for this investigation are mentioned here

A square wave on an oscilloscope screen is used as test object and is in itself an example of a vernier situation (Fig 2) It has two alternative positions In a random way and with equal chances the middle segment of the wave is displaced up or down

The size of the displacement of the middle segment can have a series of

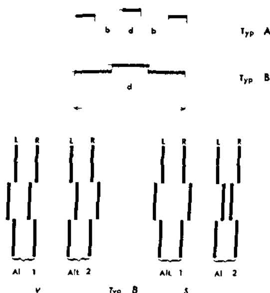


Fig 2

Two sets of test objects are used Type A and Type B each with the total extension (e) consisting of two reference lines (r) and a middle segment (d) which is displaced from the reference lines with a variable distance (a) In Type A r is kept constant (3 3 min arc) and a separation distance (b) has been varied (2 4 7 12 and 20 min arc) giving the different values of e (14 18 24 34 and 50 min arc) In Type B the same values of e have been used b = 0 r and d = 1/3 e The two test objects on the top of the figure illustrate the targets as they are seen on the oscilloscope screen without the prismatic device The four pairs of objects on the bottom of the figure illustrate the non fused images of a target Type B when it is observed with the prismatic device in vernier and stereo situation respectively

Table II

Vernier and stereo thresholds related to the extension of the target (Type B)

Extension of the target (min arc)	14		18		24		34		50	
Subject	ζ	η	ζ	η	ζ	η	ζ	η	ζ	η
G L	3 0	48 9	3 6	48 0	3 0	28 5	3 4	21 4	4 4	24 0
G S	2 8	38 6	2 5	44 8	3 /	31 5	3 3	44 8	4 7	32.5
V W	2 9	56 1	2 0	61 8	2 7	39 3	2 4	43 2	3 0	49 8
I B	2 7	48 0	4 0	38 6	5 1	32 0	5 6	24 5	4 6	°90
O W	3 0	35 1	2 7	34 4	4 1	66 6	6 4	37 2	4 3	23 0
M (n = 5)	2 9	45 3	3 0	45 5	3 7	39 6	4 2	34 2	4 2	31 7
s d	0 1	8 5	0 8	10 5	1 0	15 6	1 7	10 7	0 7	10 8

The symbols used are the same as those in Table I Thresholds in sec arc

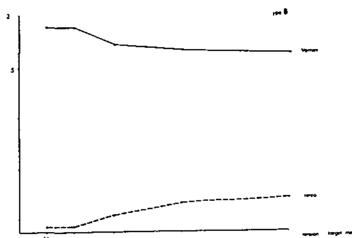


Fig 6

Curves relating the thresholds (in sec arc) of the vernier and the stereo functions to the extension (e) of target Type B Average values for 5 individuals

curve around a certain mean level When calculated on step values the dispersion is of the same order of magnitude for all the observers The standard deviation varies between 0 5 and 3 0 with an average of 1 5 2 0 The dispersion is about the same for all kind of targets and for both kinds of visual functions

Besides these fluctuations within one examination variations can also be

discrete values (steps) (a_0, a_1 ... a_ω) The ratio between two consecutive steps (a_n, a_{n-1}) is 1 2

The subject has to interpret the position of the test object and when he presses one of two buttons in front of him (one for each position) his intrepretation is transferred back to the apparatus After three consecutive and correctly interpreted choices the dislocation (a) is decreased one step (by a factor 1/1 2) If the observer cannot perceive a certain disparity – and does not press the button within a certain exposure time – *or if the position of the disparity is not* correctly interpreted the dislocation (a) is increased one step (i e by a factor 1 ²) The performance is automatically recorded and the step curve obtained denoting the sizes of the objects shown can be analyzed for instance in the way which will be described in a following section

(b) The Test Objects

Two different sets of test objects have been used for the examinations of the stereo vernier relationship (Fig 2) In type A there is a separation (b) between the reference lines and the displaced middle segment The separation (b) has been varied and the thresholds of the vernier and stereo function have been determined for five different values of b ,2, 4 / 12 20 min arc) The two reference lines (r) and the displaced part of the line (d) were all of same length (*5 3* min arc) and the total extension of the five modifications of Type A will thus be determined by the different separation distances used

The test object of type B consists of a continuous broken line The length of the displaced part is 1/3 of the total extension of the test object and the five *different modifications* used all have the same total extension as those of type A

(c) The Prismatic Device

The binocular perceived *vernier* situation originated from a square wave can be perceived as a stereoscopic one – *if certain* conditions of the test object are fulfilled – by means of a prismatic device *designed by Arakau (1967b)* in front of the observer It consists of two Dove prisms *one in front of each eye* without focal power and with the quality of rotating *an image in the frontal* plane without changing the direction of the light When a Dove prism is rotated 90 about its horizontal axis the image is rotated 180

With this prismatic device the image of the horizontally extended square wave could easily be rotated clock wise or counter clock wise In the stereo vernier *experiments* the vernier situation was always examined binocularly and with the lines of the test *object in* a vertical position (Fig 2)

To produce a stereoscopic situation from a vernier situation one of the

Table III
Binocular and Monocular Vernier Thresholds

Extension of the target (min arc)	14			18			24			34			50		
b (min arc)	2			4			7			12			20		
Subject	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye
C S	5 2	5 0	9 5	7 2	6 0	9 7	6 8	8 5	15 2	15 2	13 0	18 0	29 7	2 5 2	34 3
V W	4 3	3 8	4 7	3 8	8 6	8 8	6 8	8 7	10 5	11 2	9 2	17 7	14 3	19 3	20 3
L G	5 3	5 7	8 7	5 8	6 3	10 0	9 7	8 8	15 5	9 8	16 5	19 0	16 7	19 3	24 7
M (n = 3)	4 9	4 8	7 6	5 6	7 0	9 5	8 4	8 7	13 7	12 1	12 9	18 2	20 2	21 3	26 4
s d	0 6	1 0	[illegible]66	1 7	1 4	0 6	1 5	0 2	2 8	2 8	3 7	0 7	8 3	3 4	7 2

The eye with the best vernier performance monocularly is denoted as 1st eye Thresholds in sec arc

prisms was rotated 90° in order to present an image rotated 180° to one of the eyes (Fig 2 and 3) The displaced part of the square wave gives the transverse disparity necessary for the perception of stereopsis and the observer just has to determine whether the middle segment of the target is situated in front of the reference lines or behind them It must be observed that with this method of producing a stereo situation the pupillary distance is of no importance

The two disparate images so produced are easily fused by most observers with normal bifoveolar fixation The sum of the vernier off sets – the stereo disparity – must of course be within the limits of Panum s zone and the test object on the oscilloscope screen must be symmetric with regard to a vertical plane in the center of the target

By means of this prismatic device any type of heterophoria of the observers

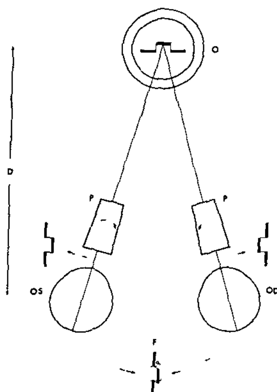


Fig 3

Schematic illustration of the method by which a stereoscopic situation is produced By means of a prismatic device (P) the images of the square wave on the oscilloscope (O) are rotated clock wise for the left eye and counter clock wise for the right eye When the images are fused a transverse disparity is produced The displaced segment of the target is perceived either in front of or behind the plane of the reference lines depending on the direction of the displacement (a)

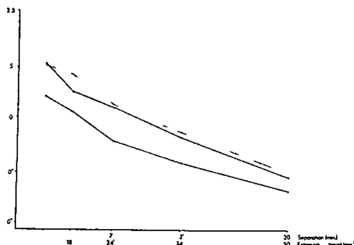


Fig 7
The relation between binocular (dotted line) and monocular (continuous lines) vernier performances The upper continuous line represents the best monocular vernier per formance (right or left eye) and the lower line the result obtained with the other eye Target Type A with different separation distances (b) has been used Average values for 3 individuals

suspected from one day to another owing to varying degrees of attention That is the reason why every subject has been re examined on a later occasion The differences between the results obtained in two identical examinations have been calculated For the different types of targets they are (in steps) Vernier (A and B) = 0 02 3 1 (M = 1 2) Stereo (A) 0 1-4 4 (M = 2 0) and Stereo (B) 0 2 6 9 (M = 3 2)

Discussion

(a) The Vernier Performances

The lowest threshold values of the vernier function for those trained subjects are obtained with the target Type B The optimal intra individual results vary between 2 0 sec arc and 3 0 sec arc (Table II) These values are in good agree ment with the results previously reported (for a review see *Foley Fisher* 1968) but a comparison with earlier results mostly obtained with a target of type black on white" and with different statistical methods must be made with caution owing to the special kind of experimental technique used in this study

Considering the results with target Type B (Fig 6) however it is apparent that in spite of the increasing length of the target there is no improvement of the vernier function If the vernier off set is 1/3 of the total length of the line most observers achieve a better performance with a shorter type of test object

eyes can be compensated This can be accomplished by changing the position of the axes of the prisms With two micrometer screws the prism axes are most carefully adjusted with regard to the optic axes of the eyes

( ) Monocular and binocular vernier functions

From experiences with the stereo vernier situation it seemed logical to study also the monocular versus the binocular vernier function

The examination of monocular and binocular vernier performances was carried out in principally the same way as previously described In a random way the subject had to interpret a vernier pattern (target Type A) with its different separation distances monocularly or binocularly In order not to produce a change of the size of the pupil in the monocular situation by occluding the contralateral eye a diffusing filter was placed in front of that eye Three experienced subjects took part in the examination

(e) Experimental arrangements

Throughout the various experiments all parts of the arrangement were kept constant. The illumination of the room (of about 15 lux) the luminance of the test object and the background illumination on the oscilloscope screen were chosen to give optimal viewing comfort and visual acuity In some of the experiments a background target consisting of concentric circles was used as a stimulus for fusion During the course of the experiments however it turned out to be unnecessary to use this fusion stimulating background since all the experiments were made in an orthophoric state of binocular vision It was found that the reference lines (r) alone were a stimulus for fusion strong enough to maintain a stable bifoveolar vision throughout the examination session.

It is known from earlier experiments (*Baker* 1949 *Foley Fisher* 1968) that vernier acuity is dependent on the wave length of illumination In this investigation the background on the oscilloscope was pale yellowish green and the test object itself had a radiant energy distribution with its maximum in the middle of the visible spectrum (5100 Å)

The subject was placed 5 m in front of the test object viewing the target through the prismatic device Uniformly illuminated unstructured screens with small apertures restricted the binocular field allowing nothing else but a field subtending 8 around the test object to be seen by the observer Due to the rotating effect of the prisms it was necessary to have a neutral surrounding visual field.

Each experimental session consisted of a stereo vernier block of 10 min (Fig 4) 5 min for each situation starting with one of the targets presented either in the vernier or stereo situation in a random way The maximum expo

contrary to the earlier findings with targets of type two peg test (*French* 1920 *Bair* 1953 *Ludvigh* 1953) If a separation distance (b) is introduced between the test details as in target Type A a definite correlation is found between the magnitude of b and the corresponding thresholds of the vernier function (Fig 5) As can be expected the narrower the separation the lower are the thresholds obtained It is in accordance with the optimal level obtained with target Type B which can be considered as a borderline case of Type A where $b = 0$

The impairment of the vernier function which was reported by some investigators (*Berry* 1948 *Ludvigh* 1953) when the reference lines (or dots) are brought close to the vernier off set – a fact difficult to explain – could not be demonstrated in the present material

(b) **The stereo performance**

It is apparent from Figs 5 and 6 that the lowest threshold values of the stereo function are obtained with a test object of Type A with the intrasubject variation between 6 5 sec arc and 9 1 sec arc The mean value for the five subjects (7 8 sec arc) is of the same order as that found with other methods (for references see *Matsubayashi* 1939 and *Graham* 1966) In earlier literature however there are no reports on stereo acuity with a test object of this vertically arranged three rod test. A somewhat lower threshold is found with the present method if the test used is arranged in accordance with Helmholtz three rod test A test object of that kind has not been used in these experiments however because there is no vernier situation comparable to this target

There are some characteristic features of the stereo curves compared with the vernier ones Contrary to the findings in the corresponding vernier situation there is an impairment of the stereo function if the angular separation (b) of the test object, Type A, is decreased from the range 4 7 min arc to 2 min arc (Fig 5) This is consistent with the breakdown of stereo obtained with the test object Type B (Fig 6) Thus it can be concluded that a separation of a definite magnitude (4 7 min arc) is necessary to obtain an optimal stereo function if the present experimental method is used

The deterioration of stereo acuity for targets with a narrow separation between the test details was also found by *Berry* (1948) who explained the stereo breakdown as probably attributable to the importance of ocular muscle balance in the depth situations This conception of a deteriorating effect on stereo acuity due to a heterophoria or an induced phoria will also be found elsewhere in the literature on the subject (*Litinsky* 1939 *Palmer* 1962) but most authors conclude that there is no correlation between stereo acuity and the degree of the heterophoria under optimal viewing conditions (*Nichols* 1950 *Sachsenweger* 1956 *Maki* 1968)



Fig
l a t l a cell nucleus at s mewhat higher magnification Intranuclearly located struc t es m rphol gically identical to herpes simplex virus are shown (arrows) × 20 600

in thin sections cut through the center of the core (Fig 3 arrow) When the re was opaque throughout the reason was generally tangential sectioning In m t cases the core was located centrally within the capsid A peripheral posi ti n oul l als be seen however (Fig 5) The mean diameter of the core was 4 0 400 Å

The apsid which is a protein shell surrounding the core was spherical or



Fig 3

Enlargement of part of Fig 2 Each virus particle consists of an inner core and an outer capsid A particle cut through the center of its core is indicated by an arrow × 60 000

slightly oval Its mean diameter was 900–950 Å In the sections it appeared as a dark ring surrounding the core

Most virus particles present in the cells of this clinically undamaged corneal

As mentioned in a *previous section any heterophoria in this investigation* was compensated by the prismatic device and cannot interfere with the results Some pilots studies on heterophoria and its relation to stereo acuity have been made with the same technique (*Stigmar* 1968 unpublished data) The stereo acuity was determined during 10 minute periods for different angles of induced heterophoria But for extreme cases when the angle was at the limit of the fusional amplitude these experiments failed to show any correlation between the heterophoria and the stereoscopic acuity

It can therefore be concluded that there is no support for the view that the stereo breakdown with narrower or no separations (b) is caused by an ocular imbalance Another explanation must be discussed

One essential factor may be the stereo deteriorating effect of contours described by *Burian* (1951) When fusion of disparate images gives rise to stereopsis there will be a shift from the primary subjective visual directions to a single visual direction Burian states that the assimilation of visual directions as they occur in stereopsis is impossible if the corresponding centers are sti mulated at the same time The result of such stimulations is that fusion is *partially lost and the character of the stereoscopic depth perception is changed* The stereoscopic vision in this situation corresponds to the range of patent stereopsis without fusion according to *Ogle* (1962) where the relationship between stereo acuity and disparity becomes less definitive

Even if there is no distinct contour in a geometric sense in the area of the resulting new visual direction when targets Type A and B are used this area is stimulated by the diffraction and aberration discs induced by the illuminated *test object The luminance distribution must also induce some* kind of lateral inhibition (*v Bel esy* 1968) In fact the closer the reference lines are situated the more these lines act as they would in a situation of two point resolution

This geometric and schematic conception of stereoscopic vision seems to be in conflict with Julesz experiments (1963) with computor generated random stereo images In these experiments it was shown that the same transverse dis parity (horizontal shift") was perceived with different qualities of stereopsis *by changing the contours or even in the absence of distinct contours* As regards the stereo pairs used in these experiments devoid of familiar cues and without recognizable disparities in a geometric sense they will still give rise to retinal images with a light distribution on corresponding retinal meridians as if a real geometric disparity existed in the stereo pairs Thus the prerequisite for stereop sis is given but the complex patterns of the objects make it difficult to analyze the various factors separately which in a secondary way might reduce the *magnitude* of depth perception

With the present method of examining stereoscopic vision no secondary cues can influence the results The pupillary distance of the subject is of no im portance for the magnitude of the stereo disparity and the size differences of



A

the vessels are not brought out by the periodic acid Schiff technique because the vessels are covered with profuse chromatophores The chromatophores contain a dark brown pigment melanin which is insoluble in water alcohol fat solvents and dilute acids and alkalis but soluble in strong alkalis and bleachable by powerful oxidising agents such as potassium permanganate (*Ogilvie* 1945 *Lillie* 1954)

Bleaching of melanin was used in the past to study the choroid vasculature after a Neoprene injection (*Ashton* 1953) Periodic acid Schiff staining without a preceding injection was applied in the present work The vessels stain light

the retinal image which have been a source of error with many of the conventional stereo measuring methods (*Graham* 1966) are eliminated here

(c) **The relationship between vernier and stereo functions**

From the previous discussion it is evident that there exists a stereo deteriorating effect, which becomes more evident with decreasing separation distances while the vernier function gradually improves under the same conditions Consequently the optimal values of the two functions cannot be the accurate basis for a comparison

From Fig 5 and 6 it can be seen that the stereo performance – for any value of b – does not yield results better than those obtained in the vernier performance contrary to the findings of *Berry* (1948)

As is clearly demonstrated in Table I and in Fig 5 there is a close consistency between the threshold values of the vernier and stereo functions for corresponding values of b in the range of b = 7 20 min arc In fact no significant difference can be shown between the threshold values for the two kinds of vision The increased spreading of the stimulating pattern (following the increasing value of b) seems to affect the two visual functions equally This close parallelism between the vernier and the stereo curves in the right part of Fig 5 makes it probable that the same measuring mechanism is involved and sets the limits of the quantitative capacity of the two visual functions which also has been suggested by *Roelofs* (1948) With this presumption further aspects on the relationship can be pointed out

The probability of perceiving the vernier off set is the same as the probability of perceiving the total stereo disparity within the range of b = 7 20 min arc But this stereo disparity is composed of two smaller vernier off sets each of them half of the total disparity That means that a stereo disparity – at threshold – can be perceived although its constituent vernier parts cannot be perceived

Consequently it can be stated that the thresholds of the vernier function are not limited by factors on the retinal level but by the capacity of higher visual centers because the retinal receptors have the capacity of detecting and codifying a vernier off set of half the magnitude of the smallest stereo disparity that can be perceived

Now the question arises if a binocularly perceived vernier off set – at threshold – can also be considered as being composed of two sub liminal monocular vernier off sets From the results in Table III and Fig 7 it can be seen that there is no significant difference between the results obtained monocularly – if the performance with the eye with the best vernier acuity is considered – and the results obtained binocularly The conclusion must be that there are no signs of an additive visual mechanism in the binocular vernier situation like that found in the comparable stereo situation

This conclusion is in accordance with the presumption earlier made that the vernier and stereo acuities are both based on the perception of the relative visual directions and furthermore – no quantitative information is being lost in the visual process where the half-images" of the two eyes are transformed into a three dimensional perception

Summary

The vernier and the stereo functions have been studied with a new automatic technique The test objects have been produced on an oscilloscope screen and identical test objects have been used for testing both visual functions The thresholds obtained are of the same magnitude as those obtained with methods previously used The main results can be summarized as follows

1 The thresholds obtained vary considerably with the shape of the test object Two different sets of test objects have been used one of them consisting of a continuous broken line (Type B) one of them consisting of three vertically arranged lines where the middle non aligned line is separated from the two reference lines by a gap (Type A) Type B yields optimal vernier thresholds but increased stereo thresholds contrary to the findings with the test object type A where a parallelism of the two visual functions can be demonstrated When the separation distances between the test details are decreased in test object Type A which thus approaches Type B a stereo deteriorating effect can be demonstrated In order to secure a maximum stereoscopic efficiency the separation distances must be within a certain range

2 The stereo vernier relationship has been studied For the test object Type A the same limiting values for both functions can be demonstrated suggesting that the thresholds for the perception of a stereo disparity and a vernier off set respectively are the same A similar basic "measuring mechanism may therefore be involved in stereoscopic vision and in the vernier situation

3 Experiments with the monocular and binocular vernier function fail to show any clear difference between the thresholds obtained monocularly with the best eye and binocularly

Acknowledgement

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vation of irideal vascular patterns and does not admit of any histological scrutiny of irideal vessels

The iris has sensory vasomotor and motor nerve fibres of which the last supplies the iris muscles They are not visible by ordinary staining methods (*Hogan & Zimmerman* 1962) For examining the finer innervation of the rab bit s iris and the irideal vasculature the iris was sectioned into flat layers and the silver carbonate method was used on formalin fixed material and the osmium zinc iodide method on fresh material (*Lassmann 1964*) In this work the myelinated afferent nerves of the pig iris are visualised in flat preparations after potassium permaganate bleaching by the periodic acid Schiff technique In frozen sections myelin of peripheral nerves stains a vivid red to red purple by the periodic acid Schiff procedure This reaction was obtained in material fixed with formaldehyde and chromated before dehydration and embedding (*Lillie* 1954)

The flat preparation of the pig iris is fairly thick Its thickness prevents more detailed study of the morphology of the vessels The preparation is therefore thinned by means of trypsin digestion This method will be described in a sub sequent work

Summary

The flat mount method for studying the vessels and the myelinated nerves of the pig iris is described With this procedure the vessels and the myelinated nerves of the iris are demonstrated by periodic acid Schiff staining after potassium permanganate bleaching The thickness of the preparation is a disadvantage of the method and trypsin digestion is therefore recommended

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chamber angle changes in eyes with retinal detachment compared to the fellow eyes the following study was performed

Material

Material I

Age and sex distribution The total number of patients with retinal detachment hospitalized in our department in the two year period 1967 1968 were 267 (128 males 139 females) with an average age of 51 8 years for males and 58 4 years for females This difference in average age is significant (Student s t test t = 3166 P < 0 01) There is also a slight female prevalence (52 1 %) but this is not significantly different from the norwegian census population (females 50 2 %)

The ratio of females to males in the different age groups is however not constant neither in the detachment material nor in the census population (Statistical Yearbook 1968) This variation in ratio is visualized in fig 1 Among the detachment patients there is a male prevalence in the lower age groups and a female prevalence in the higher age groups When compared with the census population it is however only the male prevalence in the age groups from 30

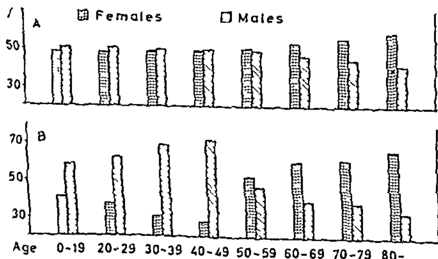


Fig 1
A Ratio of females to males in census population in the different age groups Total number = 3 8 × 10⁶ B Ratio of females to males in the age groups of retinal detachment material I Total number = 267

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From Oslo University Eye Department Rikshospitalet Oslo Norway
(Head Professor dr med Thore Lie Thomassen)

TRAUMA AND RETINAL DETACHMENT

The anterior chamber angle with special reference to width, pigmentation and traumatic ruptures

BY

PER SYRDALEN

Traumatic ruptures in the anterior chamber angle are frequently seen as a result of ocular contusion (*Tonjum* 1966) When these changes are seen in eyes with retinal detachment they may be taken as proof of previous ocular contusion (*Wolff & Zimmerman* 1962 *Cox et al* 1966) A history of trauma is very often reported by retinal detachment patients and it would be of interest to know the incidence of chamber angle ruptures due to contusion in these eyes

Gonioscopic findings in eyes with retinal detachment have been reported by *Sebestyen et al* (1962) but chamber angle lesions due to contusion were not dealt with by these authors and the incidence of these changes in eyes with retinal detachment has not yet been evaluated

Pigmentation of the anterior chamber angle occurs more frequently with advancing age both in normal and in glaucomatous eyes (*Zuege et al* 1967) and more frequently in glaucoma capsulare than in eyes with primary open angle glaucoma (*Horven* 1966) As retinal detachment is a disease of age and also a disease seen in connection with trauma eye surgery uveitis and other eye diseases angle pigmentation is not expected to be less in detachment eyes than what seen in a normal population

In order to get more information about width pigmentation and traumatic

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From the Eye Clinic University of Helsinki
(Head Professor Salme Vannas M D)

FLAT PREPARATION METHOD FOR STUDYING BLOOD VESSELS AND MYELINATED NERVES OF THE PIG IRIS

BY

MATTI SAARI

Because of the laminar structure of the eye flat preparations afford an unusually favourable opportunity to study such structures as retinal and choroidal vessels corneal and trabecular endothelium lens epithelium and retinal pigment epithelium The periodic acid Schiff technique has been used earlier for flat mount staining of the retina (*Friedenwald* 1949 *Ashton* 1949) Alone periodic acid Schiff staining is incapable of demonstrating the iris vessels and the myelinated nerves in flat preparations as the iris is rather thick and contains profuse melanin in chromatophores and in the pigment epithelium However melanin of the choroid can be bleached with heavily oxidising potassium permanganate (*Ashton* 1953) A method based on these procedures for the demonstration of the vessels and the myelinated nerves of the pig iris by the flat mount technique is described in this paper

Material and Methods

Pig eyes from an abattoir were used in the study After enucleation the eyes were fixed in 10 per cent neutral formalin for a minimum of 24 hours The eyes were opened equatorially The vitreous and the lens were removed with

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Table I

Norwegian census population (total 3 766 000) in different age groups Ratio females/males in census population among retinal detachment patients (material I 267 and material II = 227 patients) and among traumatic cases from material II (36 patients) N = number of patients (n) = number of patients each age group

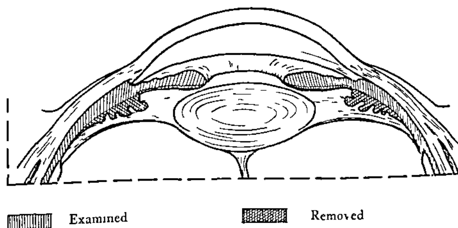
Age groups (years)	0–19	20–29	30–39	40–49	50–59	60–69	70–79	80–
Census population × 10⁻⁴ Norway 1966	1 [illegible]35	499	409	505	461	363	216	78
Ratio females/males	0 949	0 953	0 972	0 994	1 025	1 139	1 240	1 400
Ratio females males Material I	0 700	0 600	0 444	0 389	1 115	1 [illegible]26	1 600	2 000
N = 267 (n)	(17)	(16)	(13)	(25)	(55)	(96)	(39)	(6)
Inhabitants per one detachment per year	79 91[illegible]	34 316	34 [illegible]08	[illegible] 220	9220	4160	6092	14 300
Ratio females/males Material II	0 400	1 000	0 667	0 4[illegible]9	1 000	1 486	2 000	4 000
N = 227 (n)	(14)	(12)	(10)	(20)	(46)	(87)	(33)	(5)
Ratio females males Traumatic cases	0 000	0 500	1 000	0 333	0 600	0 286	0 000	0 000
N = 36 (n)	(5)	(3)	(4)	(4)	(8)	(9)	(2)	(1)

forceps and scissors The iris ciliary body and anterior choroid were freed in toto The residue of the vitreous and the pigmentary layer of the iris were wiped off carefully with pieces of blotting paper The ciliary process was cut away with small scissors as completely as possible (Fig 1) It was washed overnight in several changes of distilled water It was then kept in 0 25 per cent potassium permanganate solution for four hours and washed in water kept in 5 per cent oxalic acid solution for six min and washed in running water for 10 min and finally washed in distilled water The preparation was floated on a slide, dried and stained with PAS hematoxylin For control purposes a part of the irises were halved one half was stained without bleaching with PAS hematoxylin and the other half was stained after bleaching with PAS hematoxylin

Results

The blood vessels and myelinated nerves were covered with profuse chromatophores in an unbleached iris and hardly any details of the vessels and nerves could be demonstrated (Fig 2)

In a bleached iris chromatophores were not seen The vessels of the iris were visible The major arterial circle of the iris and the radial vessels stained purple Capillaries were not visualised however (Fig 3) The myelinated afferent nerves were clearly brought out by the periodic acid Schiff technique



Examined Removed

Fig 1

A drawing of the anterior part of the eye showing the anterior uvea used in the study and the ciliary process to be removed

to 49 years which may be considered statistically significant (30 39 years chi square = 6 448 $P < 0\ 05$ 40 49 years chi square = 9 101 $P < 0\ 01$)

In table I is listed the ratio of females to males in the age groups in the *census population in retinal detachment material* (I) and the estimated ratio of inhabitants to one detachment per year This estimate is based on the assumption that our department treat roughly 55 % of all patients hospitalized with retinal detachment in Norway In the age group 0 19 years there is one detachment per about 80 000 inhabitants per year The incidence then gradually increases up to the age group 60 69 years where there is one detachment per about 4000 inhabitants per year Over 70 years the incidence seems to decrease a little This decrease of incidence may well be artificial The patients are old some of them will not be seen by a doctor and some will not be hospitalized due to their high age

Material II

A personal examination of all patients by the author was necessary to obtain uniformity in the criteria used to classify trauma angle width chamber angle pigmentation *and traumatic chamber angle ruptures Due to vacations however*, this could be performed only in 85 % (227 patients = material II) of the total number of retinal detachment patients (material I) hospitalized in our department in the two year period

There is no major difference in age and sex distribution between material I and material II In material II 106 patients (46 7 %) were males with an average age of 52 2 years and 121 patients (53 3 %) were females with an average age of 59 3 years The ratio of females to males in the age groups in material II is listed in *table I and the sex distribution in the different age groups in material* I and material II are illustrated in fig 2

The following presentation of the material refers to material II

Both sexes show an insignificant prevalence to left eye (table II) detachment (53 7 %) Redetachment in previously operated eye is seen in 2 2 % and bilateral detachment in 7 5 % of the cases

Trauma The different forms are listed in table III The numbers in the table are mainly based on the predetachment case history given to the author from each patient *All patients were inquired for ocular trauma blows to the* head or accidents prior to detachment The age distribution is seen in fig 2 (C) There is no significant difference in average age between females (47 4) and males (45 6 years) in this group There is however a highly significant difference (chi square = 12 45 $P < 0\ 001$) in the ratio of males to females of the traumatic compared with the nontraumatic cases the traumatic cases thus yielding a large prevalence of males

1 *Perforating injury* Four of these eyes had suffered severe (+ + table IX)

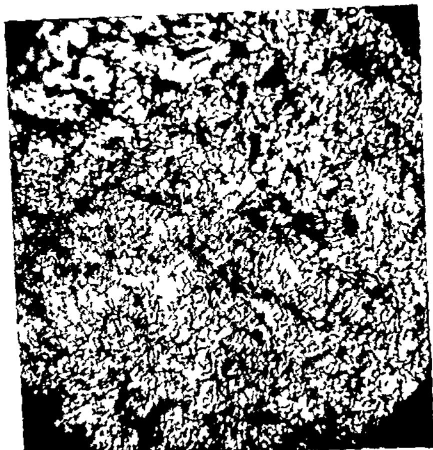


Fig 9
Flat preparation Unbleached iris of the pig Chromatophores obscure the vessels and the myelinated nerves PAS hematoxylin × 100

in a bleached pig iris The myelinated nerves stained dark red purple There was a rich plexus of myelinated nerves in the bleached iris of the pig (Fig 3)

The flat preparation of the pig iris was however fairly thick and often worked loose on staining Its thickness prevented a more detailed study of the morphology of the vessels

Discussion

The retinal vessels have earlier been studied in flat preparations by the periodic acid Schiff technique (*Friedenwald* 1949 *Ashton* 1949) In an unbleached iris

Table III

Material II Trauma in predetachment history N = 36 (*males* = 27 *females* = 9) One male is listed both as perforating injury (3½ years before detachment) and ocular contusion (*13 days before detachment*) Both trauma were severe but the contusion precipitated the detachment.

	Males	Females	Total
Previous perforating injury	5 (4 7 %)	0	5 (2 2 %)
Ocular contusion	18 (17 %)	5 (4 1 %)	23 (10 1 %)
Indirect trauma	5 (4 7 %)	4 (3 3 %)	9 (4 %)
No trauma in history	9 (74.5 %)	112 (92 6 %)	191 (84 1 %)

with secondary endophthalmitis In this eye vitreous changes and retinal degeneration were found upon admission but no *other sign of previous perforating* injury could be seen Due to the severeness of the symptoms after a perforating injury it is not likely that cases belonging to this group have been overlooked

2 *Ocular contusion* has been classified into three degrees of severity + (minor ocular contusions or contusions where little information about degree is available) ++ (more severe contusions where the patients have given detailed information about the accident) and +++ (severe contusions with hyphaema intravitreal bleeding or other obvious signs of contusion)

In the ocular contusion group are listed patients previously hospitalized due to ocular contusion (++ 1 +++ 5) seen by ophthalmologist because of ocular contusion but not being hospitalized (+ 1 ++ 1 +++ 1) giving a history of ocular contusion immediately followed by visual disturbances (+ 1 ++ 3 +++ 1) and patients reporting ocular contusion not seen by ophthalmologist and not giving visual disturbances or discomfort afterwards (+ 3 ++ 1)

17 % of the males and 4 1 % of the females gave a history of ocular contusion prior to detachment (Minor injuries such as lesions in the conjunctiva corneal abrasions or anamnestic negligible ocular contusions without any symptoms afterwards are not listed as trauma in the table)

3 *Indirect trauma* In this group are listed patients giving a history of blows to the head (5) or eye surroundings (4) followed by visual disturbances The time interval between the indirect trauma and the beginning of symptoms has been from immediately after the trauma and up to 3½ months

The time interval between the actual trauma and the occurrence of detachment is listed in table IV

Some possible complicating factors seen in material II in detachment eyes



A

the vessels are not brought out by the periodic acid Schiff technique because the vessels are covered with profuse chromatophores The chromatophores contain a dark brown pigment melanin which is insoluble in water alcohol fat solvents and dilute acids and alkalis but soluble in strong alkalis and bleachable by powerful oxidising agents such as potassium permanganate (*Ogilvie* 1945 *Lillie* 1954)

Bleaching of melanin was used in the past to study the choroid vasculature after a Neoprene injection (*Ashton* 1953) Periodic acid Schiff staining without a preceding injection was applied in the present work The vessels stain light

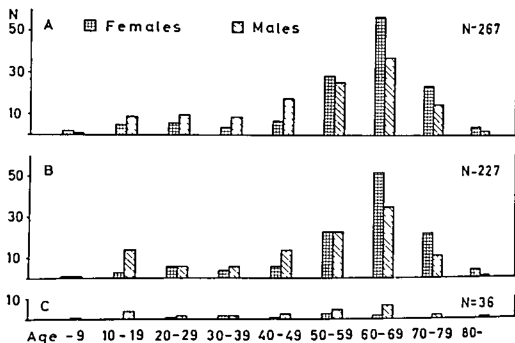


Fig 2

Age and sex distribution A material I (N = 267) B material II (N = 227) and C patients with trauma in predetachment history from material II (N = 36)

Table II

Material II Distribution right/left eye detachment Redetachment in previously operated detachment eye Previously operated detachment in fellow eye Bilateral detachment upon admission and total number of bilateral detachments N = 227 (males = 106 females = 121)

	Males	Females	Total
Detachment right eye	50 (47 2 %)	59 (48 8 %)	109 (48 %)
Detachment left eye	59 (55 7 %)	63 (52 1 %)	122 (53 7 %)
Redetachment	2 (1 9 %)	3 (2 5 %)	5 (2 2 %)
Prev operat detach fell eye (a)	8 (7 5 %)	5 (4 1 %)	13 (5 7 %)
Bilateral detach upon admission (b)	3 (2 8 %)	1 (0 8 %)	4 (1 8 %)
Total number of bilat detach (a + b)	11 (10 4 %)	6 (5 %)	17 (7 5 %)

perforating injuries due to metallic intraocular foreign body (2) and rupture of the bulb after blunt trauma (2) The fifth eye had a needle perforation (+)



B

Fig 3A and B

Fig 3A Flat preparation. A bleached iris of the pig The vasculature and the myelinated nerves of the iris are visualised by the periodic acid Schiff technique The major arterial circle of the iris (MC) and the radial vessels (V) have stained purple The long posterior ciliary nerve (CN) and the myelinated nerves of the iris (N) have stained dark red purple PAS hematoxylin × 40

Fig 3B The same preparation as in Fig 3A Chromatophores are not seen as in Fig 2 The radial vessels (V) and the myelinated nerves (N) are visualised PAS hematoxylin × 100

purple in bleached irises But the capillaries are not visualised This method makes it possible to observe histologically complete irideal vessels which can not be seen in serial sections of the iris But this method prevents clear obser

to know the incidence of pseudoexfoliation among patients suffering from retinal detachment in order to evaluate if any difference excists between detachment eyes and fellow eyes

In table VI are listed the results of a chi square test on the factors mentioned above of possible importance for the development or precipitation of retinal detachment. Of these only aphakia and angle ruptures are seen to be of importance

Material III

Selected material From material II all eyes harbouring eye diseases or possible complicating factors other than the actual detachment i e trauma, previous eye surgery glaucoma, uveitis and pseudoexfoliation are excluded Material III thus includes only patients with primary untreated uncomplicated retinal detachment in one eye and the other eye is apparently healthy This selection has been done in order to evaluate the possible influence on chamber angle pig

Table VI

Material II Number of detachment eyes and fellow eyes with a history of uveitis presence of aphakia and pseudoexfoliation previously diagnosed glaucoma and presence of traumatic chamber angle ruptures Results of chi square on the incidence in detachment eyes and fellow eyes

	Detachment eyes	Fellow eyes	Chi square	Significance level
Uveitis +	15	13		
Uveitis —	212	214	0 038	–
Aphakia +	27	9		
Aphakia —	200	214	8 719	P < 0 01
Pseudoex +	7	9		
Pseudoex —	220	218	0 065	–
Glaucoma +	8	7		
Glaucoma —	219	220	0 000	–
Angle rupt. +	13	0		
Angle rupt —	210	209	10 644	P < 0 01



Fig 4

Part f the cytoplasm (upper left corner) and part of the nucleus of another cell in the m l p thel um Many intranuclearly located virus particles are seen. × 93 500

epithelium were found within the nuclei The cytoplasm of these cells contained very few structures that could be identified as virus particles The picture of the cells lining the active lesion was quite different A very large number of

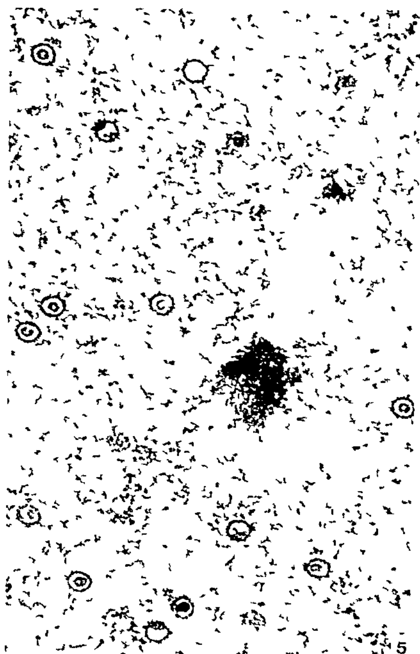


Fig 5

Enlargement of part of Fig 4 The material of the core is sometimes seen to be excentrically located × 58 000

virus particles were generally seen both in the cytoplasm and in the nucleoplasm

Extracellularly located virus particles in most cases surrounded by an additional envelope derived from cellular membranes were frequently seen in re

Table IV

Time interval between actual trauma and retinal detachment N = 36 (males = 9, females = 9) One patient is listed as (+ 1) in the perforating injury group (over 6 months) but the actual trauma was ocular contusion (0 4 weeks) Se text table III

	Perforating injury	Ocular contusion	Indirect trauma
0– 4 weeks	1	10	/
4–12 weeks	0	2	0
12 weeks – 6 months	1	4	2
Over 6 months	2 (+ 1)	7	0

Table V

Material II Possible complicating factors in detachment eyes and fellow eyes N = 227 (males = 106 females = 121) One male fellow eye had been enucleated (tumor) but had previously been otherwise healthy (percentages calculated in relation to N = 106 in fellow eye group too)

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
Uveitis in hist	8 (7 6 %)	7 (5 8 %)	15 (6 6 %)	7 (6 6 %)	6 (5 %)	13 (5 7 %)
Aphakia	14 (13 2 %)	13 (10 7 %)	27 (11 9 %)	5 (4 7 %)	4 (3 3 %)	9 (4 %)
Pseudoexfoliation	3 (2 8 %)	4 (3 3 %)	7 (3 1 %)	4 (3 8 %)	5 (4 1 %)	9 (4 %)
Glaucoma Prim + sec	5 (4 7 %)	3 (2 5 %)	8 (3 5 %)	3 (2 8 %)	4 (3 3 %)	7 (3 1 %)

and fellow eyes are listed in table V Included are a history of uveitis (6 6 % 5 7 %) aphakia (11 9 % 4 %) pseudoexfoliation of the lens capsule (3 1 % 4 %) and glaucoma (3 5 % 3 1 %) (previously diagnosed and under treatment)

Pseudoexfoliation is as retinal detachment a disorder of age A relationship between the two disorders is not known It would therefore be of some interest

5 Gonioscopy is of importance to prove the existence of previous ocular contusion

6 Traumatic retinal detachment (all forms) usually occurs in predisposed patients judged in relation to the condition of the fellow eye

Summary

A two year retinal detachment material of 227 cases is presented The role of aphakia glaucoma uveitis and pseudoexfoliation is evaluated Gonioscopic findings concerning chamber angle width pigmentation and traumatic angle lesions are studied 55 6 % of the male and 60 % of the female patients reporting ocular contusion had chamber angle lesions The role of trauma and predisposing factors to retinal detachment is discussed

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Table V II

Material II The nter o cl ambe angle W dil p gme tatı n and t u t c angle le n G nio copy n 2"3 d tach nent eyes (males = 10 females = 118) a d 209 fell w ey s (males = 97 females = 11)

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
Crade 0 (cl sed)	1 (1 %)		1 (0 5 %)			
Open Gr I II		1 (0 9 %)	1 (0 5 %)		2 (1 8 %)	2 (1 %)
O en Cr III IV	104 (99 %)	117 (99 1 %)	2?1 (99 %)	97 (100 %)	110 (98 ? %)	?07 (99 %)
None/little pigment	72 (69 2 %)	86 (7? 9 %)	158 (71 2 %)	73 (75 3 %)	92 (82 1 %)	165 (79 %)
Mo lerate pigm	14 (13 5 %)	?3 (19 5 %)	37 (16 7 %)	10 (10 3 %)	15 (13 4 %)	25 (1? %)
Heavy pigm	18 (17 3 %)	9 (7 6 %)	27 (12 1 %)	14 (14 4 %)	5 (4 ? %)	19 (9 %)
Angle lesion	10 (9 5 %)	3 (2 ? %)	13 (5 8 %)			

were confirmed by *Regan & Rousseau* (1966) and they concluded that retinal detachment may occur in eyes in which the rate of aqueous flow and also the facility of outflow are primarily abnormal and that the detachment is not necessarily the cause of the altered hydrodynamics" An imbalance was suggested in the physiology of aqueous production and the normal mechanisms of outflow and absorption and this imbalance was found to be bilateral in some cases even if the detachment occurred only in one eye

Our present knowledge indicate therefore that the hypotony frequently seen in eyes with retinal detachment is caused by a decreased formation of aqueous humor even sometimes also associated with decreased facility of outflow (*Dobbie* 1963 *Becker* 1963 *Regan & Rousseau* 1966)

Normally there is little difference in intraocular pressure between two healthy eyes of an individual (*Davanger* 1965) Individuals with an untreated retinal detachment in one eye and an apparently healthy other eye give excellent opportunity to use the other eye as control

The aim of the present investigation is to study intraocular pressure in retinal detachment eyes to evaluate possible relationship between intraocular pressure and area of detachment duration of detachment and number of retinal holes Of interest is also the pre operative ocular rigidity and the difference in intraocular pressure obtained by use of Schiotz tonometer and Goldmann applanation tonometer

Material

The present investigation is performed on two groups of patients

Group A This group consists of 124 patients (46 males and 78 females) with an average age of 57 6 years (10 87) There is no significant difference in average age for females (58 9 years) and males (55 4 years)

21 (45 7 %) of the male and 28 (35 9 %) of the female patients were classified as myopic (i e refraction minus 0 5 or more) and among these 7 males and 6 females had myopia minus 8 or more

Group B This group consists of 37 patients (16 males and 21 females) with an average age of 57 3 years (17 79) As judged by the result of the Student s t test (t = 1 996 0 05 < P < 0 10) there is no significant difference in average age for females (61 6 years) and males (51 8 years)

7 of the males (43 8 %) and 2 of the females (9 5 %) were myopic and of these 3 males and 1 female exceeded minus 8

Group A patients were hospitalized during 1967 1968 and group B patients during 1969 All patients included in this investigation had primary retinal detachment (unoperated) in one eye and the other eye was apparently healthy

mentation of the above mentioned factors Material III includes 134 patients (51 males and 83 females)

Methods

All detachment eyes and fellow eyes (material II and III) were examined under the same conditions Gonioscopy was performed with mydriasis obtained by topical use of *Cyclogyl* 1 % (Cyclopentolate hydrochloride) and metaoxedrin chloride 10 % A Goldmann three mirror contact lens and a *Haag Streit* 900 slit lamp were used throughout

The width of the filtration angle was classified from Grade IV (wide open) to Grade 0 (closed) as described by *Sebestyen et al* (1962) Grade IV means an angle in which the ciliary body band is visible throughout the whole circumference Grade III means that the ciliary body band is invisible but the scleral spur is visible In Grade II the scleral spur is invisible but the posterior part of the trabeculum is visible In Grade I only part of the anterior trabeculum is visible and Grade 0 means an angle closed up to Schwalbe s line Grade IV III corresponds to *Scheie s* (1957) Grade 0 wide open – Grade II narrow

The pigmentation in the chamber angle was classified in three groups

1 *None/little pigmentation* which corresponds to *Scheie s* (1957) none pigmentation 2 *Moderate pigmentation* which corresponds to Grade I II pigmentation by Scheie and 3 *Heavy pigmentation* which corresponds to Scheie s Grade III IV This classification was thought to be sufficiently accurate due to the fact that all eyes both detachment and fellow were examined by the author and the same criteria used each time

Traumatic chamber angle ruptures were classified after criteria given by *Wolff & Zimmerman* (1962) and *Tonjum* (1966) Tears of the anterior face of the ciliary body or iris root were taken as proof of previous ocular contusion These changes may be difficult to discover if a long time has passed since the trauma In this material the fellow eye served as control in the majority of patients Only eyes in which the traumatic changes were clearly seen (and the other eye had no such changes) were listed in the traumatic angle lesion group

Pseudoexfoliation of the lens capsule was determined under full mydriasis and the use of slit lamp

Results

Material II Table VII shows the results concerning chamber angle width pigmentation and traumatic chamber angle ruptures Gonioscopy was performed

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From Oslo University Eye Department Rikshospitalet Oslo Norway
(Head Professor dr med Thore Lie Thomassen)

INTRAOCULAR PRESSURE AND OCULAR RIGIDITY IN PATIENTS WITH RETINAL DETACHMENT

I Preoperative study

BY

PER SYRDALEN

Retinal detachment is usually accompanied by hypotony *Kleiner* (1933) reviewed the literature and reported results of own investigation He stated that 75 % of all detachment eyes had intraocular pressure lower than the healthy other eye The hypotony increased with increasing time since the detachment occurred increased with increasing area of detachment and was more pronounced in eyes with numerous and great ruptures in the retina Acute and very extreme hypotony may accompany retinal detachment (*Beigelman* 1929) but a more moderate hypotony is the rule Some detachment eyes will have raised intraocular pressure and even if the association of open angle glaucoma and retinal detachment is unusual (*Becker* 1963) it has been reported (*Lawton Smith* 1963 *Sarin et al* 1963 *Guillaumat & Bonnin* 1967)

The cause to the hypotony has not been explained by any change in ocular rigidity in detachment eyes (*Ytteborg* 1961 *Rousseau & Regan* 1965 *Regan & Rousseau* 1966) neither has the existance of an extraordinary outflow channel through the retinal detachment or retinal breaks been proved (*Dobbie* 1963 *Regan & Rousseau* 1966)

By using fluorescin technique and suction cup *Dobbie* (1963) found evidence of decreased formation of aqueous humor in detachment eyes These results

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Table VIII

Material III The anterior chamber angle Width and pigmentation in selected part of material II N = 134 (males = 51 females = 83)

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
Open Gr I II					1 (1 2 %)	1 (0 7 %)
Open Gr III IV	51 (100 %)	83 (100 %)	134 (100 %)	51 (100 %)	82 (98 8 %)	133 (99 3 %)
None/little pigm	40 (78 4 %)	66 (79 5 %)	106 (79 1 %)	39 (76 5 %)	69 (83 1 %)	108 (80 6 %)
Moderate pigm	5 (9 8 %)	14 (16 9 %)	19 (14 2 %)	5 (9 8 %)	11 (13 3 %)	16 (11 9 %)
Heavy pigm	6 (11 8 %)	3 (3 6 %)	9 (6 7 %)	7 (13 7 %)	3 (3 6 %)	10 (7 5 %)

were confirmed by *Regan & Rousseau* (1966) and they concluded that retinal detachment may occur in eyes in which the rate of aqueous flow and also the facility of outflow are primarily abnormal and that the detachment is not necessarily the cause of the altered hydrodynamics" An imbalance was suggested in the physiology of aqueous production and the normal mechanisms of outflow and absorption and this imbalance was found to be bilateral in some cases even if the detachment occurred only in one eye.

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7 of the males (43 8 %) and 2 of the females (9 5 %) were myopic and of these 3 males and 1 female exceeded minus 8

Group A patients were hospitalized during 1967 1968 and group B patients during 1969 All patients included in this investigation had primary retinal detachment (unoperated) in one eye and the other eye was apparently healthy

on 223 (105 males 118 females) detachment eyes and on 209 (97 males 112 females) fellow eyes Four detachment eyes (aphakia – 2 aphakia and uveitis – 1 uveitis – 1) and eighteen fellow eyes (apparently normal eye – 2 enucleated – 1 previous perforating injury – 3 previous uveitis and phtisic bulb – 6 complicated cataract – 1 previously operated detachment – 3 uncomplicated cataract – 2) were not gonioscopically examined The majority of these eyes were greatly pathological and in some of them gonioscopy was impossible to perform Pathologic chamber angle would be expected in most of these eyes

The results from the selected material (material III) are listed in table VIII

Chamber angle width Both table VII and VIII show open chamber angle (Grade IV + III) in almost 100 % of detachment eyes and fellow eyes In table VII, one male eye is listed as closed angle This eye had a serious contusion with hyphaema iris dialysis traumatic cataract followed by closed angle secondary glaucoma and finally retinal detachment

Chamber angle pigmentation In male detachment eyes and fellow eyes there is a higher incidence of heavy pigmentation than in the corresponding female groups (table VII and VIII) A higher incidence of heavy pigmentation (both sexes) is also seen in detachment eyes compared to fellow eyes (table VII) If all eyes harbouring complicating disorders (table II III V) are excluded however the higher incidence of heavy pigmentation in detachment eyes is eliminated

Chamber angle ruptures 9 5 % of the male and 2 5 % of the female detachment eyes harbour these changes All these patients reported ocular contusion prior to detachment

In table IX is listed a summary of some factors considered to be of importance when dealing with patients with some sort of trauma in predetachment history The table is based on the case history the type and severity of trauma and the result of gonioscopy and biomicroscopy (three mirror lens) in each traumatic case from material II Biomicroscopy was not performed in 3 fellow eyes (enucleated – 1 cataract – 1 child lack of cooperation – 1)

Comment

A male prevalence in retinal detachment materials is the usual finding (*Schepens & Marden* 1961) but equal distribution among the sexes or female preponderance (*Edmund* 1964) has also been reported A slight female prevalence (52 1 %) is seen among our total number of patients with retinal detachment in the two year period When using the census population as basis it is however a statistically significant male prevalence in the age groups from 30 49 years The male overrepresentation in these groups may partly be due to the higher

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incidence of trauma among the males but other sex differences are possibly *also of importance* The female prevalence observed in the higher age groups of retinal detachment patients is not statistically significant due to the corresponding change in ratio females to males in the general population The average age for males is 6 6 years younger than for females and the female concentration in the higher age groups is more prominent than the male

The effect of senescence is however seen in both sexes where the age group from 60 69 years comprises the highest number of patients This can also be illustrated by the estimated ratio of inhabitants per one detachment per year The calculation is possible due to the small number of eye departments in Norway and because the average number of retinal detachments treated each year in these departments is roughly known The incidence in the age groups varies as expected greatly from 1 detachment per about 80 000 inhabitants (0 19 years) to 1 detachment per about 4000 inhabitants (60 69 years) per year Similar results have been reported by *Bohringer* (1950) who also found the highest incidence in the age groups from 60 69 years

The data obtained concerning age and sex relationship among the patients with retinal detachment from our department are in very good accordance with the data given by *Schepens & Marden* (1961 and 1966)

Material II includes 85 % of the total number of patients with retinal detachment from our department over a two year period which were personally examined by the author It is not likely that this selection has induced major differences in the results since the composition of material II is very close to the basic material from which it is extracted

Bilateral detachment is in material II seen in 7 5 % of the patients The incidence vary in the literature but is given from Scandinavia by *Tornquist* (1963) – 15 5 % *Edmund* (1964) – 9 5 % *Braathen* (1968) – 5 8 %

Aphakic detachments range from 7 to 25 % in series of retinal detachment (*Norton* 1964) and it is commonly accepted that aphakia gives increased risk towards retinal detachment The incidence of aphakia among detachment eyes (11 9 %) and fellow eyes (4 %) in material II support this view The difference is statistically significant at the 1 % level a fact which actually proves the increased risk

Pseudoexfoliation of the lens capsule is found in 3 1 % of detachment eyes and in 4 % of fellow eyes All patients (10) in which pseudoexfoliation was seen belong to the age groups over 60 years (125 patients) giving an incidence of 8 % This is in accordance with *Aasved's* (1969) incidence of pseudoexfoliation in normal populations over 60 years The presence of pseudoexfoliation of the lens capsule will therefore not indicate any increased risk to retinal detachment

Glaucoma diagnosed and treated prior to admission was seen in 4 4 % of all patients in material II with no difference between detachment eyes (3 5 %)

each time to avoid inexactitude which arises when using Friedenwald s nomo gram

The time since detachment occurred (group A) was determined as exactly as possible in days based on the information given to the author by each patient A HAFF Planimeter 315 was used on the drawing made from each detachment eye and the detached area in per cent of the total area was calculated The pur pose of using this method was of course only to give a rough measure and not the exact area since it is impossible to transfer the fundus of an eye to a plane surface in this way

All eyes were examined with the indirect ophthalmoscope (Schepens type) and the three mirror Goldmann lens but it is only the results (number of rup tures) from group A that are dealt with (in connection with hypotony of the eyes) in this paper

Results

Group A Table I shows the distribution of eyes with intraocular pressure higher in detachment eye than in fellow eye (12 9 %) equal intraocular pres sure both eyes (27 4 %) and lower intraocular pressure in detachment eye than in the other eye (59 7 %) There is no major differences between the sexes in this distribution

Table II shows the intraocular pressure in mm Hg (arithmetic mean in de tachment eyes and fellow eyes Intraocular pressure in fellow eyes is 1 98 mm

Table I

Group A Intraocular pressure (Schiotz tonometry) in detachment eye higher than in the fellow eye equal intraocular pressure both eyes and lower intraocular pressure in detachment eye than in the fellow eye in per cent of number of eyes in males (46 pa tients) females (78 patients) and total (124 patients)

	Intraocular pressure		
	higher in detachment eye than in fellow eye	equal in both eyes	lower in detachment eye than in fellow eye
Males	10 9 %	26 1 %	63 %
Females	14 1 %	28 2 %	57 7 %
Total	12 9 %	27 4 %	59 7 %

Table IX

Summary of some of the factors considered to be of importance among the traumatic cases from material II
N = 36 (males = 27 females = 9)

		Detachment eyes									Fellow eyes				
		No of eyes with									No of eyes with				
		Number of patients	Angle lesion	Retinal degenerat	Oral dialysis	Arrow head rupt	Round holes	Prev ret detach	Family detach	Myopia	Posterior vitr detach / vitr degenerat	Retinal degenerat	Prev ret detach	Arrow head rupt	Round holes
Perforating injury	+	1		1			1				1	1			
	++	4		3	3						2	2		1	
Ocular contusion	+	10	4	8	4	3	4		1	3	6	7			
	++	6	4	3	2	4	3				4	3			
	+++	7	5	2	4	1	2				3	2			1
Indirect trauma		9		6	1	6	5	1		2	5	4	3	1	2

There has been no previous surgery or injury, no previous diagnosed glaucoma or inflammation neither to the eyes with detachment nor to the fellow eyes Gonioscopy revealed wide open chamber angle in all eyes

Methods

All patients were examined by the author Tonometry was performed with the same certified Schiotz tonometer on all eyes in group A and with another certified Schiotz tonometer on all eyes in group B The same applanation tonometer (Goldmann s model Haag-Streit) was used on all patients in group B Applanation tonometry was performed in the sitting position immediately followed by Schiötz tonometry in the lying position using 5 5 Gm plunger weight

Tonometry in group A was performed before any mydriatics or cycloplegics were given and before any procedure was done which could alter intraocular pressure However some detachment eyes had received atropine by the referring ophthalmologists but usually the time between instillation of atropine and tonometry exceeded 24 hours Group A patients came walking to the examination room and were examined the first day upon admission

Group B patients had all both eyes dilated by topical instillation of Cyclogyl 1 % (Cyclopentolate hydrochloride) and metaoxedrin hydrochloride 10 % at least 30 minutes before tonometry These patients were lying in bed with bin oculus and were transported to the examination room in the bed They were all examined the day after admission

The differences in tonometry procedure and use of mydriatics in group A and B were partly the result of local circumstances however all patients in each group were examined under the same conditions

Corneal anesthesia was obtained by topical use of oxibuprocain 0 2 %

Intraocular pressure in mm Hg was taken from Friedenwald s 1955 table using the nearest 0 5 scale reading on the Schiötz tonometer Applanation values were read to the nearest 0 5 mm Hg Readings were taken from right eye - left eye until a constant value was obtained (approximately 2 4 readings each eye)

Ocular rigidity was calculated with the formula

$$K = \frac{\log P_t - \log(\text{appl ton} + 1)}{V_c \ 0\ 44}$$

(*Ytteborg* 1960) K = rigidity coefficient P_t = intraocular pressure during tonometry (Friedenwald s 1955 table) V_c = volume of corneal indentation during Schiotz tonometry (Friedenwald 1955) and 0 44 mm^3 = corneal indentation caused by applanation tonometry (*Goldmann & Schmidt* 1957) K was calculated

to detachment, but an accident can also be proven by the presence of the anterior chamber angle lesions seen in the present study in 55 6 % of male (60 % of female) detachment eyes in which there has been a history of contusion *Tonjum* (1966) found traumatic chamber angle ruptures in 94 3 % of eyes with primary traumatic hyphaema. Since the incidence in the present study is not so high some of the contusions reported must have been of a minor degree A detection of retinal dialyses will also point toward a traumatic genesis This view is supported from the present study in which dialyses were found in 4 7 % of the nontraumatic and in 36 1 % of the traumatic detachment eyes

When considering trauma (perforating injuries ocular contusions indirect trauma or combination of these) as cause to retinal detachment it is necessary to have in mind 1 The severeness and type of the actual trauma 2 The known disposition of the patient to retinal detachment (family bilateral) 3 The disposition of the patients eyes to retinal detachment (judged after a thorough examination including biomicroscopy both eyes) As to the last point the pre existing condition of the detachment eye is usually not detected but an examination of the fellow eye will give usefull information about predisposing factors It will be seen from table IX that even in the perforating injury group (average age 27 6 years) the fellow eyes is not healthy Only one eye in this group was considered to be without predisposing factors In the ocular contusion and indirect trauma groups four fellow eyes were considered healthy These *results support the view that traumatic retinal detachment is rare in a* healthy eye (*Gruber* 1963)

The present investigation has shown a definite relationship between aphakia and retinal detachment and between chamber angle ruptures and retinal detachment No such relationship has been proved for previously diagnosed glaucoma or uveitis

Conclusions

1 The incidence of pseudoexfoliation is equal in detachment eyes and fellow eyes and the same as expected in a normal population within the same age groups
2 Angle pigmentation is found to be of the same degree in detachment eyes and fellow eyes when eyes harbouring complicating factors are excluded
3 Gonioscopy has revealed wide open chamber angle in nearly 100 % of detachment eyes and fellow eyes
4 Diagnostic mydriasis in these patients will not produce acute closed angle glaucoma

Table III

Group A. Intraocular pressure (i o p) in fellow eyes and detachment eyes (mm Hg Schiotz) area of detachment (in per cent of a total retinal detachment) in relation to duration of detachment in days N = number of patients in each group

Duration in days	i o p detachment	i o p fellow	difference	% detachment.	N
1	15 80	15 54	+ 0 26	44 04	5
2	15 92	16 64	— 0 72	55 34	5
3	13 58	14 83	— 1 25	44 33	4
4	10 92	12 0	— 1 08	49.33	10
5	12 01	15 72	— 3 71	60 94	10
6 + 7	10 94	13 43	— 2 49	55 94	11
8 + 9	10 59	13 59	— 3 0	49 06	9
11 + 12 + 13	9 86	12 44	— 2 85	61 0	7
14	9 35	12 35	— 3 0	69 76	12
15–20	11 72	12 88	— 1 17	60 50	6
21–29	10 22	12 25	— 2 04	74 56	11
30–60	12 72	14 05	— 1 33	68 36	13
61–180	11 10	13 35	— 2 25	0 20	15
270–720	13 05	13 23	— 0 18	70 90	6

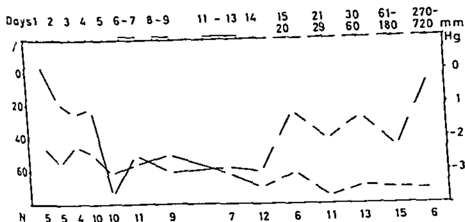


Fig 1

Table III is visualized in this figure ×—× Average difference in intraocular pressure between detachment eyes and fellow eyes —— Average area of detached retina.

Ruptures or holes in detached retina were found in approximately the same degree whether the detachment was fresh or longstanding There was not found any relationship between degree of hypotony and number of ruptures In 5 eyes

and fellow eyes (3 1 %) Between 1 and 2 % of the population over the age of 40 may have glaucoma (for references see *Duke-Elder* 1969) and the incidence increases with age According to this the incidence of glaucoma among the detachment patients is not especially high and the concept that glaucoma (or treatment with miotica) may cause retinal detachment is not supported

The *anterior chamber angle* has been found wide open in nearly 100 % of all examined eyes with no difference between the sexes The anterior chamber is generally deeper in males than in females (*Tornquist* 1953) but the depth has not been measured in the present study and the difference between the sexes is therefore not ruled out Another factor considered to be of more importance to the present results of chamber angle width, is the possible effect of cyclo plegia Gonioscopy has in all eyes been performed under mydriasis The cyclo plegic effect of Cyclogyl will make the anterior chamber deeper (*Busacca* 1955) and increase chamber angle width due to decrease in ciliary body size backward movement of iris and flattening of the lens surface This effect has been noticed by the author in some eyes where gonioscopy was performed before and after mydriasis was obtained

The degree of widening of the anterior chamber angle has however not systematically been evaluated but is not thought to be of a magnitude that would cause considerable change in the results from the present study

The concept is therefore given that wide open chamber angle is a usual finding among patients suffering from retinal detachment No case of acute closed angle glaucoma has been seen or precipitated among these patients and mydriatics may thus be used in detachment eyes with little or no risk of angle closure It could also be suggested that patients with shallow angle or closed angle glaucoma are less prone to develop retinal detachment than patients with deep anterior chamber and wide open anterior chamber angle This is in agree ment with *Cibis s* (1965) hypothetical combinations of various sizes of the eye versus various sizes of the hyaloid body and the disposition to retinal detach ment

Angle pigmentation No major difference in degree of pigmentation is found between detachment eyes and fellow eyes As expected the degree of pigmen tation is reduced when eyes harbouring complicating factors are excluded A difference is however seen between male and female eyes in the heavy and moderate pigmentation groups but whether this difference is real or only a result of inaccuracy in estimating the degree of pigmentation is not clear

Trauma Retinal detachment due to trauma most commonly is seen in males (*Thiel & Kilian* 1963 *Cox et al* 1966) and this is significantly shown also in the present study

The time interval between trauma and detachment varies (table IV) but a long interval does not exclude trauma as possible cause When there has been a perforating injury there is seldom any question about trauma being the cause

Hg higher (average) than in detachment eyes This difference is significant (judged by the Student's t test which also will be applied to results later on t = 6 831 P < 0 001) There is also a significant difference (2 1 mm Hg) between female and male detachment eyes (t = 2 831 P < 0 01) and between female and male fellow eyes (1 19 mm Hg t = 1 991 P < 0 05)

In table III are listed average intraocular pressure and difference between fellow eyes and detachment eyes in relation to days duration of detachment The corresponding average area of detached retina in each group is tabulated and fig 1 visualize the results

The average area of detached retina is seen to increase rapidly the first days after occurrence of detachment then is followed by a more slow increase as time pass on

The average hypotony in detachment eyes compared to fellow eyes is most pronounced from 5 to 14 days after the occurrence of detachment After this time hypotony is reduced

Table IV will also illustrate the distribution of detachment eyes with intraocular pressure higher equal to and lower than the fellow eyes in three groups in relation to duration of detachment The differences (mm Hg arithmetic mean) between fellow and detachment eyes are listed in table V Between 5 and 14 days duration this difference is highly significant (P < 0 001) None of the other differences reach the 5 % level of significance

The area of detached retina over 15 days duration is significantly greater than the area up to 14 days duration (P < 0 005)

It is thus shown that hypotony is greatest from 5 to 14 days after the occurrence of detachment and that area of detachment is greatest in cases with 15 days duration or more A direct relationship between area of detachment and degree of hypotony has not been found

Table II

Group A Intraocular pressure (I o p = arithmetic mean in mm Hg Schiotz) in detachment eyes and fellow eyes N = number of eyes s d = standard deviation of population

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
N	46	78	124	46	78	124
I o p	10 22	12 32	11 54	12 77	13 96	13 52
s d	4 186	3 654	3 976	3 395	3 115	3 222

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Table V

Group A Difference between intraocular pressure in detachment eyes and fellow eyes (Schiotz) in relation to duration of detachment (in days) Area of detachment (in per cent of a total retinal detachment) in the groups and t values (Student s t test) Significance levels N = number of patients

N	Duration in days	Difference	t value	sign level	Area of detachment		t value	sign level
24	0– 4	— 0 76	0 645	–	48 7 %	56 1 %	3 134	P < 0 005
49	5–14	— 2 97	4 371	P < 0 001	58 3 %			
30	15–60	— 1 56	1 600	–	69 2 %	69 7 %		
21	61–	— 1 65	1 479	–	70 4 %			

lation to the active lesion Such extracellular virus particles were not found in the clinically undamaged areas of the corneal epithelium studied in the present investigation

Discussion

Identification of structures as beeing virus particles was done on the basis of following facts 1 The structures were similar in morphology to herpes simplex virus of known strain studied in tissue cultures (13 15) 2 The structures were found mainly within the cell nuclei The DNA containing core (5) of herpes simplex virus is known to replicate within the nucleus (5 9 11 13) Although normal cytoplasmic structures may sometimes resemble virus particles normal nuclei never contain such structures 3 For one of the patients isolation of virus as well as serological tests were performed Both ways the presence of an infection with herpes simplex virus was proven The purpose of the present investigation was to study the distribution of virus particles in human corneal epithelium by comparing areas with active lesions to clinically undamaged areas Previous work on rabbit corneal epithelium (7 17 18) was based on inoculation experiments and is not likely to reflect the situation in human after spontaneous infection A precise knowledge of the location in relation to the active dendritic lesions of the biopsies taken is essential This was made possible by carefully dissecting out strips of corneal epithelium under visual control in the split lamp microscope Scraping the cornea in order to obtain minimal flakes of tissue (14) is in this respect unsatisfactory An improvement of the tissue preservation as compared to that of an earlier study of human dendritic keratitis (16) also contributed to the possibility of a more precise analysis of the cells involved

In a previous report on dendritic keratitis (14) and in the present paper it has been shown that virus particles may be present in a very large number of cells in undamaged areas of the corneal epithelium The lack of enveloped extracellular virus particles the very low number of virus particles in the cytoplasm and the fairly low number of intranuclearly located virus paricles as compared to the picture of the dendritic lesion are indications that the infection might be of different degree of activity in different areas of the corneal epithelium It seems that the rate of replication of virus particles is very high in the dendritic lesions and very low or perhaps absent in other areas This finding is in agreement with other evidence in the literature that herpes simplex virus might lie dormant in the tissue Kaufman Brown & Ellison (8) studied sections of lacrimal gland and conjunctiva with fluorescein - labelled antibody to herpes simplex virus and showed that virus antigen was present in four of seven

patients with clinically inactive disease Anderson Margruder & Kilbourne (1) demonstrated that herpes simplex virus could be reactivated in healed rabbit corneal lesions in connection with induction and evocation of local hypersensitivity of the Arthus type It is well known that recurrences of herpes simplex keratitis in human are common 25 % of the patients suffer a recurrence within two years (2) It appears that a reactivation of a dormant infection may be the explanation of the frequent recurrences What causes a reactivation in human is not known Neither is it known why only certain areas of the corneal epithelium develop dendritic ulcers

Since we now know that in herpetic keratitis also the undamaged areas of the corneal epithelium may contain virus the treatment of the disease ought not to be restricted to the active lesions The use of topical idoxuridine thus provides a good alternative If chemical cauterization with tincture of iodine of the dendritic lesions is beeing used or if the epithelium containing the lesions is beeing mechanically removed it is recommendable to combine such measures with the use of topical idoxuridine This might possibly reduce the risk of recurrences and of spread of the virus The presence in the corneal stroma of particles which are apparently herpes simplex virus was demonstrated in an electron microscopic investigation of human chronic herpetic keratitis (3) and the actual spread of sich particles to the corneal stroma (18) and to corneal nerves (4) was shown in inoculation experiments on rabbits The presence of herpes like particles in the iris was shown in connection with kerato iritis (21)

Summary

Biopsies of human corneal epithelium in herpes simplex keratitis were studied in the electron microscope Areas containing active dendritic lesions were compared with respect to virus content and distribution to areas of clinically undamaged corneal epithelium located two to five mm away from the closest lesion Large amounts of virus particles were observed in the nuclei as well as in the cytoplasm of the cells lining the active lesions A finding of interest was the fact that also the majority of the cells of the clinically intact epithelium contained intranuclearly located virus particles although fewer The possible significance of this observation in relation to the questions of dormant infection recurrence of the disease spread of virus and treatment of the disease is discussed

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Table IV

Group A Intraocular pressure (Schiotz) in detachment eye higher than in the fellow eye equal intraocular pressure in both eyes and lower intraocular pressure in detachment eye than in the fellow eye in relation to duration (in days) of detachment Average area of detached retina (in per cent of a total retinal detachment) in each group N = number of patients

N	Duration in days	Intraocular pressure			Area of detachment
		higher in detachment eye than in fellow eye	equal in both eyes	lower in detachment eye than in fellow eye	
24	0– 4	25 %	29 2 %	45 8 %	48 [illegible] %
49	5–14	6 1 %	24 5 %	69 4 %	58 3 %
51	15–	15 7 %	47 %	37 3 %	69 7 %

no rupture or hole in detached retina was detected The average hypotony in these eyes were 2 8 mm Hg

Group B The results concerning ocular rigidity and intraocular pressure (applanation and Schiotz tonometry) are listed in table VI Ocular rigidity is insignificant lower in detachment eyes than in fellow eyes A significant difference is seen between ocular rigidity in females and males both in detachment ($t = 2\ 230$ $P < 0\ 05$) and fellow ($t = 2\ 394$ $P < 0\ 05$) eyes

As found in group A intraocular pressure in detachment eyes generally is lower than in fellow eyes The number in group B are however too small to yield significance

The average applanation values are higher than the Schiotz values The difference in detachment eyes is 1 23 mm Hg and in fellow eyes 1 05 mm Hg

Comment

Both group A and B consists of patients selected from our department The aim has been to reduce factors with possible influence on intraocular pressure as much as possible therefore only paired eyes without any other known disorder besides retinal detachment in one eye are used

Among retinal detachment patients the average age for females is usually higher than for males (*Schepens & Marden* 1961 *Syrdalen* 1970) This is also the situation in group A and B

Intraocular pressure Retinal detachment is usually associated with hypotony

Table II

Intraocular pressure (P_o) in mm Hg in fellow eyes and operated detachment eyes in groups in relation to time after operation N = number of patients in each group Numbers in brackets = standard deviation of population

Method of operation	Interval since operation (days)	N	Applanation tonometry P_o fellow eyes	Applanation tonometry P_o detach eyes	Applanation tonometry P_o fell – P_o detach	t value* sign level	Schiotz tonometry P_o fellow eyes	Schiotz tonometry P_o detach eyes	Schiotz tonometry P_o fell – P_o detach
Group A Encircling procedures	9– 14	9	15 33 (1 23)	10 56 (3 58)	4 77	4 560 $P < 0\ 005$	13 61 (2 01)	2 79 (2 05)	10 82
	19– 54	9	14 50 (3 83)	10 83 (2 66)	3 67	2 507 $P < 0\ 05$	13 41 (3 96)	3 88 (1 89)	9 53
	61–1020	24	14 77 (3 25)	12 83 (3 93)	1 94	2 747 $P < 0\ 02$	14 59 (2 46)	5 47 (3 97)	9 12
	total	42	14 85 (3 02)	11 92 (3 70)	2 93	5 082 $P < 0\ 001$	14 13 (2 74)	4 56 (3 41)	9 57
Group B Local buckling procedures	10– 33	5	13 60 (2 30)	11 20 (1 48)	2 40	3 359 $P < 0\ 05$	14 71 (2 41)	7 68 (1 78)	7 03
	69– 150	8	15 00 (3 57)	13 38 (2 49)	1 62	1 713 –	14 19 (3 07)	11 37 (2 32)	2 82
	total	13	14 46 (3 12)	12 54 (2 36)	1 92	3 065 $P < 0\ 01$	14 39 (2 74)	9 95 (2 77)	4 44

* Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

ous production and that the greatest reduction could be found if eyes with detachment of 5 to 14 days duration were examined The hypotony may be caused by an aqueous production shock which it takes some days to see the result of and which lasts for about ten days at maximum Afterwards aqueous production to a certain extent is regained but as hypotony persists other factors of influence on ocular hydrodynamics still may be present

Ocular rigidity No significant difference is found between detachment eyes and fellow eyes and this is in agreement with results reported by *Ytteborg* (1961) *Rousseau & Regan* (1965) and *Regan & Rousseau* (1966) In the present study there is however a difference in ocular rigidity between males and females This difference is probably due to the high percentage of myopic patients in the male group as ocular rigidity decreases with increasing degree of myopia (*Castren & Pojola* 1962) Average age and intraocular pressure is higher in females than in males This may have reduced the difference in ocular rigidity between males and females a little since ocular rigidity will decrease with increasing age (*Ytteborg* 1960a) and with increasing intraocular pressure (*Ytteborg* 1960b)

Fellow eyes An interesting result of the present investigation is the low average intraocular pressure in all fellow eyes *Graham & Hollows* (1964) found average Schiotz pressure in males (age 50 to 64 years) to be 14 5 14 6 mm Hg and in females (same age) to be 15 8 15 9 mm Hg They also found applanation values in average to be 1 mm Hg higher than Schiotz values The average intraocular pressure in fellow eyes (group A and B) in the present study varies from 2 to 3 5 mm Hg below these normal values The reason to this rather low pressure is not quite clear It may be a support to the statement from *Regan & Rousseau* (1966) that an imbalance in the physiology of aqueous production and the normal mechanisms of outflow and absorption exists in these patients

The use of mydriatics in group B is not the reason since the same result is seen in group A where no mydriatics were used However mydriatics in group B may have had some influence on intraocular pressure since the difference between average group A (13 52 mm Hg) and B (11 95 mm Hg) is significant ($t = 2\,608$ $P < 0\,01$) It is also possible that the difference in examining procedure (walking patient group A patients lying in bed group B) may be of some importance in this respect

Applanation Schiotz values It is usual to find that applanation tonometry yields higher values than Schiotz tonometry (using Friedenwald s 1955 table) (*Lawton Smith* 1961) *Graham & Hollows* (1964) found the difference to be about 1 mm Hg and the same has been found in the present study The change from sitting to lying position will induce a rise in intraocular pressure from 1 to 2 mm Hg (or even more) (for references see *Hetland Eriksen* 1966) The values for intraocular pressure given in Friedenwald s 1955 table must therefore be too low compared to the applanation values and the difference has been shown

tation, average 253 days) and in group B (examination from 69 to 150 days after operation, average 113 days)

Comment

In the present investigation the *fellow eyes serve as controls* A comparison of the results is only valid between detachment eyes and corresponding fellow eyes *and not between the detachment eyes in the different groups* as the numbers are small and differences in age sex and refraction will give such a comparison limited value

Ocular rigidity Sources previously referred to have shown that different forms of ocular surgery leads to reduced ocular rigidity The decrease in K may be reversible (*Lavergne* 1959) and this view is supported by the results from the present study (group B) In these eyes the destruction on the eye wall *is restricted to a limited area As postoperative ocular hyperemia* (which in itself produces reduction in K (*Ytteborg* 1960)) disappears and reparative mechanisms are finished ocular rigidity increases again In group A however the reduction in K *is permanent* K *is extremely low* in the first postoperative period and continues to stay low even if a small raise is seen Postoperative ocular hyperemia and reparative mechanisms may influence K in group A as in group B but the main reason to the permanently very low K in group A is believed to be the encircling element per se

The cerclage produces a permanent disconfiguration of the eye which leads to a decrease in intraocular volume During Schiotz tonometry a certain volume is indented in the cornea and a deformation of the posterior part of the eyeball takes place The volume of fluid displacement brought about in this way (V_t) (for references see *Hetland Eriksen* 1965) is normally made room for by distension of the eye walls by expulsion of blood from the choroid and by aqueous outflow *In cerclage operated eyes part of V_t may be given room for by the* volume increase (ΔV) an elongation of the cerclage (ΔC) will produce as the intraocular pressure goes from P_o (intraocular pressure before tonometry) to P_t (intraocular pressure while the tonometer rests on the eye) ΔV will add to normal mechanisms which serve to give room for V_t In this way higher scale readings are obtained on the Schiotz tonometer demonstrating a decrease in ocular rigidity Mathematically ΔV may be calculated using the model eye shown in fig 1 and the volume within the cerclage cylinder If h = 3 mm and r_1 = 9 mm $\Delta V = 0.2353\ \Delta C^2 + 27\ \Delta C$. *Fig 2 demonstrates the relationship* between ΔV and ΔC

Intraocular pressure The low ocular rigidity in these eyes leads to erroneous results if scale reading Schiotz is converted into mm Hg intraocular pressure

Table VI

Group B Ocular rigidity (K) applantation (Appl) and Schiotz (Sch) tonometry (mm Hg) in males females and total Detachment eyes and fellow eyes N = number of patients s d = standard deviation of population

	Detachment eyes			Fellow eyes		
	males	females	total	males	females	total
N	16	21	37	16	21	37
K	0 0154	0 0187	0 0173	0 0164	0 0194	0 0181
s d	0 0045	0 0045	0 0045	0 0032	0 0045	0 0045
Appl	12 50	11 62	12 0	12 88	13 10	13 0
s d	5 09	4 26	4 59	2 85	3 59	3 75
Sch	10 26	11 15	10 77	11 0	12 67	11 95
s d	4 63	3 76	4 12	2 88	3 32	3 91

(*Kleiner* 1933 *Huerkamp* & *Behme* 1955 *Ytteborg* 1961 *Beeler* 1963 *Dobbie* 1963 and many others) and the present investigation has only confirmed this

The hypotony is usually moderate the first days after the occurrence of detachment (fig 1) between 5 and 14 days it is at maximum and after this time it subsides gradually This finding concerning the older detachments is in agreement with *Sebestyen et al* (1962) who found that postoperative elevation of ocular pressure was related to duration of the retinal detachment and that longstanding cases may have a tendency toward glaucoma In the present series of retinal detachment there has however not been detected any cases of glaucoma neither in fresh nor in older detachments

Kleiner (1933) and *Dobbie* (1963) found increasing hypotony with increasing size of retinal detachment and Kleiner did also notice that the hypotony was less marked the first days after the occurrence of a detachment than afterwards To some degree the present investigation show similar results but it has been shown (fig 1) that there is not a direct relationship between average area of detachment and average degree of hypotony The hypotony follows some days after the occurrence of detachment and decreases after a period at maximum even if area of retinal detachment gradually increases as time pass on

The present study has not shown any direct relationship between number of retinal holes or area of detachment and hypotony of the eye Decreased formation of aqueous humor has already been shown to exist in detachment eyes (*Dobbie* 1963 *Beeler* 1963 *Regan* & *Rousseau* 1966) but the present study would indicate that there might be considerable variation in the rate of aque

Table II

Intraocular pressure (P_o) in mm Hg in fellow eyes and operated detachment eyes in groups in relation to time after operation N = number of patients in each group Numbers in brackets = standard deviation of population

			Applanation tonometry				Schiotz tonometry		
Method of operation	Interval since operation (days)	N	P_o fellow eyes	P_o detach eyes	P_o fell – P_o detach	t value* sign level	P_o fellow eyes	P_o detach eyes	P_o fell – P_o detach
Group A Encircling procedures	9– 14	9	15 33 (1 23)	10 56 (3 58)	4 77	4 560 $P < 0\ 005$	13 61 (2 01)	2 79 (2 05)	10 82
	19– 54	9	14 50 (3 83)	10 83 (2 66)	3 67	2 507 $P < 0\ 05$	13 41 (3 96)	3 88 (1 89)	9 53
	61–1020	24	14 77 (3 25)	12 83 (3 93)	1 94	2 747 $P < 0\ 02$	14 59 (2 46)	5 47 (3 97)	9 12
	total	42	14 85 (3 02)	11 92 (3 70)	2 93	5 082 $P < 0\ 001$	14 13 (2 74)	4 56 (3 41)	9 57
Group B Local buckling procedures	10– 33	5	13 60 (2 30)	11 20 (1 48)	2 40	3 359 $P < 0\ 05$	14 71 (2 41)	7 68 (1 78)	7 03
	69– 150	8	15 00 (3 57)	13 38 (2 49)	1 62	1 713 –	14 19 (3 07)	11 37 (2 32)	2 82
	total	13	14 46 (3 12)	12.54 (2 36)	1 92	3 065 $P < 0\ 01$	14 39 (2 74)	9 95 (2 77)	4 44

* Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

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tonometry is therefore strongly recommended for intraocular pressure assessment on operated retinal detachment eyes

Sources previously referred to have stated that reattachment of the retina fails to restore intraocular dynamics to normal The results of the present investigation support this view

Conclusions

1 Following retinal detachment surgery ocular rigidity (K) is reduced

2 Following local buckling procedures this reduction to some extent is reversible

3 Following encircling operations with silicone rubber band the reduction in K is permanent.

4 A small elongation of the encircling element will give room for an increased corneal indentation volume (Schiötz tonometry) This may indicate that the encircling element per se and the disconfiguration of the eye which is produced are the main reasons to the extremely low K

5 Retinal detachment surgery is followed by hypotony of the eye (applanation)

6 This hypotony is gradually reduced with time after operation

7 Encircling procedure produce a more pronounced early postoperative hypotony than does a local buckling procedure

8 A large Schiotz – applanation disparity is seen in operated retinal detachment eyes.

9 Applanation tonometry is recommended to be used to assess intraocular pressure level in operated retinal detachment eyes

Summary

The results on ocular rigidity and intraocular pressure (Schiotz applanation) are presented for 55 successfully operated retinal detachment patients Ocular rigidity is largely and permanently reduced following encircling procedures Following local buckling procedures the low ocular rigidity to some degree is reversible Hypotony is seen after retinal detachment surgery The hypotony is reduced as time pass on after operation but intraocular pressure in detachment eyes will as a rule not reach the level of fellow eyes

to be 5 mm Hg when both procedures were performed in the lying position (*Hetland-Eriksen* 1966)

Intraocular pressure females – males In group A a significant lower intra ocular pressure was found in males than in females both in detachment eyes and fellow eyes *Graham & Hollows* (1964) found a similar difference but there is no obvious explanation to this fact Among the detachment patients the higher incidence of myopia among males may have some influence on the re sults but since ocular rigidity has not been calculated in this group the degree can not be established The difference in average age is too small to yield such a difference in intraocular pressure

Conclusions

1 Retinal detachment induce hypotony of the eye
2 The hypotony is most pronounced 5 to 14 days after the occurrence of de tachment and then decreases
3 The hypotony is not proportional to area of detachment
4 The hypotony is not proportional to number of retinal holes
5 No difference is found in ocular rigidity between detachment eyes and fellow eyes
6 Average intraocular pressure in fellow eyes is 2 to 3 5 mm Hg lower than what expected in a normal population This may indicate altered hydrody namics in the eyes of these patients even before detachment occurred
7 The average intraocular pressure in males is about 1 mm Hg lower than in females
8 Applanation values in sitting position are generally 1 mm Hg higher than Schiotz values in lying position This finding strongly indicate that the P_0 values listed in Friedenwald s 1955 table are too low

Summary

Two groups of retinal detachment patients without any other eye disorder neither in detachment eye nor in fellow eye are examined

Group A Relation between intraocular pressure area of detachment dura tion of detachment and number of retinal holes among 124 patients are dealt with

Group B Schiotz and applanation tonometry and ocular rigidity in 37 pa tients are dealt with

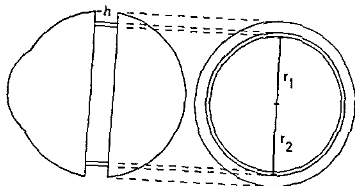


Fig 1

Schematic drawing of a cerclage operated eye in sagittal and frontal projection r_1 = radius of the circle made by the *cerclage* before tonometry r_2 = radius of the sam circle during tonometry h = height (width of) the buckle made by the cerclage

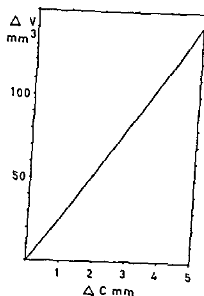


Fig 2

Volume increase (ΔV mm³) of cerclage cylinder (see text) corresponding to elongation (ΔC mm) of cerclage

using Friedenwald s 1955 table Applanation values may be several mm Hg higher than Schiötz values (table II) The results of applanation tonometry on eyes with very different ocular rigidity (such as the present results) are very little influenced by this difference due to the small volume of corneal indentation produced by this method (0 442 mm³ *Goldmann & Schmidt* 1957) and the corresponding small raise in intraocular pressure during tonometry Applanation

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CORNEAL INDENTATION PULSE AND RETINAL DETACHMENT PRE AND POSTOPERATIVE STUDY

BY

PER SYRDALEN

Hydrodynamically the vascular bed of the eye may be divided into a non pulsatile and a pulsatile part The blood flows through the non pulsatile part at a constant volume per time unit in diastole and in systole while the pulsatile part receives blood in systole This excess of blood entering the eye in systole will according to its volume (ΔV) and the intraocular pressure level initiate a corresponding increase in intraocular pressure (ΔP) Pulsesynchronous variations in intraocular pressure was first recognized by *Weber* in 1850 and may be studied in detail by various methods (*Suzuki* 1962 *Davanger* 1963 *Castren & Lavikainen* 1963 *Bynke & Krakau* 1964 *Bron et al* 1967) of which dynamic tonometry (*Horven* 1968) is used in the present study

Clinically the corneal pulse amplitudes will vary with the size of ΔV Decrease in amplitudes is seen by occlusion of the common or internal carotid artery (*Ytteborg* 1960 *Castren & Lavikainen* 1963 *Bron et al* 1967) during general anesthesia (*Horven & Syrdalen* 1970) during retrobulbar anesthesia (*Syrdalen & Horven* 1970) during tachycardia (*Horven & Syrdalen* 1970) in giant cell arteritis (*Horven* 1970c) and in choroidal degenerations (*Bynke & Schele* 1967 *Horven* 1970b) Increase in corneal pulse amplitudes has been seen in Sturge Weber s syndrome (*Flage & Horven* 1970) during bradycardia (*Horven & Syrdalen* 1970) during pain attacks of cluster headache (*Broch et al* 1970) by arteriovenous shunts (*Horven* 1970b) by choroidal melanomas (*Hor*

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INTRAOCULAR PRESSURE AND OCULAR RIGIDITY IN PATIENTS WITH RETINAL DETACHMENT

II Postoperative study

BY

PER SYRDALEN

Retinal detachment is usually accompanied by hypotony of the eye (*Kleiner* 1933 *Syrdalen* 1970) This hypotony is possibly the result of the decreased aqueous humor formation which has been shown to exist in these eyes (*Dobbie* 1963) It has also been shown that hypotony reduced aqueous humor formation and abnormally low outflow facilities are present in both eyes of many patients with unilateral nontraumatic retinal detachment. This suggest an underlying pathology common to both eyes which probably precede the detachment (*Becker* 1963 *Rousseau* & *Regan* 1965 *Regan* & *Rousseau* 1966 *Langham* & *Regan* 1969) This imbalance which exists in the physiology of aqueous formation and outflow facility in retinal detachment eyes will last after an operation Reattachment of the retina thus fails to restore intraocular dynamics to normal (*Lozano Elizonda* & *Schepens* 1968 *Bietti* 1968)

Glaucoma may be seen in association with retinal detachment (*Sebestyen et al* 1962 *Sarin et al* 1963 *Laxton Smith* 1963) Usually factors present before detachment operation (previous ocular trauma glaucoma aphakia or uveitis) or complications following detachment surgery (choroidal detachment

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with closure of filtration angle goniosynechiae uveitis) may explain such a glaucoma.

A factor which may be of importance when dealing with postoperative intra ocular pressure in retinal detachment eyes is the ocular rigidity (K = rigidity coefficient) K is not constant but differs little in the two healthy eyes of the same individual Prior to retinal detachment operations there has not been found any difference in K between detachment eyes and fellow eyes (*Ytteborg* 1961 *Aly* 1964 *Rousseau & Regan* 1965 *Regan & Rousseau* 1966 *Langham & Regan* 1969 *Syrdalen* 1970) but different forms of ocular surgery including retinal detachment operations may lead to reduced K (*Draeger* 1959 *Lavergne* 1959 *Ytteborg* 1961 *Aly* 1964 *Pemberton* 1969)

In an earlier investigation (*Syrdalen* 1970) preoperative intraocular pressure (Schiotz tonometry and applanation tonometry) and ocular rigidity in detach ment eyes and fellow eyes were studied In the present investigation the post operative course is studied

Material and Methods

The present investigation took place during 1969 All patients included in this study have been hospitalized and operated in the eye department Rikshospita let Oslo due to primary retinal detachment in one eye and with a fellow eye without retinal detachment Prior to admission there had been no form of surgery neither to detachment eyes nor to fellow eyes Cases with trauma in history glaucoma or uveitis are excluded Only eyes successfully operated are included and all eyes had wide open anterior chamber angle visible by gonio scopy The patients were examined at different intervals after operation (range from 9 to 1020 days) and all examinations were performed by the author The criteria used in the selection of patients limited the total number

The operation methods were local full thickness scleral buckling procedure encircling procedure (cerclage) or a combination of the two methods Diathermy or cryosurgery were used to produce chorioretinal adhesions Silicone rubber implant(s) were used to local buckling procedures usually without drainage of subretinal fluid (*Custodis* 1960 *Weidenthal* 1967) The encircling procedures were performed with a flat silicone rubber band of 2 mm width The principles for this method including release of subretinal fluid as given by Schepens (for references see *Schepens* 1968) have mainly been followed Eyes operated with scleral resection or trap door procedure or eyes treated solely with local dia thermy or local cryosurgery procedure are not included in the present series

The material is divided into two groups of patients according to the opera tion performed

surgery alone. Chorioretinal adhesions had been obtained either with the use of diathermy (19 patients) or cryosurgery (20 patients).

19 patients were examined both pre- and postoperatively and are thus included both in the pre- and in the postoperative dynamic tonometry group.

Methods

Dynamic tonometry is performed with the patient in supine position. The equipment consists of an electronic Schiotz tonometer, an amplifier unit and a recorder (for closer description, see *Horven* 1968). The Schiotz tonometer yields an output of 1 mV per μ plunger movement. In the present study the 5.5 Gm plunger weight was used throughout. Eye tension in scale reading Schiotz was recorded (right eye – left eye) using sensitivity setting 20 mV) and converted into mm Hg intraocular pressure using Friedenwald's 1955 table. Corneal indentation pulse amplitudes were recorded using sensitivity setting 2 mV (right eye – left eye) and 1 mV. Usually the size of the corneal indentation pulse amplitudes were calculated as an average of 5 to 10 representative waves. Corneal indentation pulse amplitudes (μ) were converted into mm³ change in ocular volume (ΔV) at the actual intraocular pressure level using converting table based on Langham – Hetland Eriksen's data as given by *Horven* (1970a).

Preoperative dynamic tonometry was performed on the day of surgery or from 1 to 3 days prior to operation. *Postoperative dynamic tonometry* was performed at an average of 121.5 days after operation (range from 7 days and up to 2 years). (In the cerclage group the interval between operation and dynamic tonometry was in average 157.8 days (range 7 to 480 days) and in the local buckling group 107.3 days (range 9 days and up to 2 years)).

In the present study, dynamic tonometry was performed before any procedure was done which would alter intraocular pressure considerably. However, both in the preoperative and in the postoperative examined patients some difference between detachment eyes and fellow eyes was present in the use of cycloplegics and mydriatics, but this difference seems to have had very little influence on intraocular pressure and corneal indentation pulse amplitudes.

Results

In table 1 the results of pre- and postoperative dynamic tonometry are summarized. The difference between detachment eyes and fellow eyes are statistically

Group A

Encircling procedure This group includes 42 patients with an average age of 57 5 years (range from 16 to 79 years) In this group 18 patients were operated with cerclage alone and 24 patients with cerclage plus sircular or meridional silicone rubber implant(s)

Group B

Local buckling procedure This group includes 13 patients with an average age of 58 5 years (range from 39 to 70 years)

Tonometry (Schiötz and applanation) and calculation of rigidity coefficient (K) is performed as previously described (*Syrdalen* 1970) The 5 5 Gm plunger weight on the Schiötz tonometer was preferred due to the fact that heavier weights gave scale readings over 20 in a great number of the cases

Results

In table I and II a summary of the results is listed The results obtained from those operated with cerclage and those operated with cerclage plus silicone rubber implant(s) were not significantly different These cases are therefore put together in the tables as the encircling procedure group Each patient is listed once even if two or more examinations are done postoperatively The results from the latest postoperative examination are used in the tables

Ocular rigidity A marked reduction in K is seen in all postoperative periods in group A In group B K is also significantly reduced but this reduction is to a certain degree reversible In group A 9 patients were examined on two different occasions The first examination (from 9 to 45 days postoperatively average 16 4 days) gave K in detachment eyes = 0 0047 (s d = 0 0014) The second examination (from 30 to 155 days after operation average 93 7 days) gave K in the same detachment eyes = 0 0065 (s d = 0 0017) This increase in K is statistically significant (as judged by the method of paired comparison t = 3 629 P < 0 01) The corresponding K in fellow eyes on the first and second postoperative examination was 0 0212 (s d = 0 0034) and 0 0203 (s.d = 0 0031)

Intraocular pressure (applanation) There is hypotony in all groups of detachment eyes after operation The intraocular pressure is at the lowest level immediately after operation and the greatest hypotony is seen in group A Hypotony is reduced as time pass on but is still present more than 60 days after operation both in group A (examination from 61 to 1020 days after ope

ven 1969) and by elevation to 40 50 mm Hg of intraocular pressure (*Hörven* 1970b)

The ocular rigidity (K = rigidity coefficient) is expected to be of importance to the size of corneal pulse amplitudes as suggested by *Bron et al* (1967) and *Bynke* (1968) The relationship between ΔP and ΔV with different size of K has been illustrated by *Davanger* (1964) in his mechanical model of an eye If the theoretical considerations based on the mechanical model is valid for human eyes corneal pulse amplitudes should be expected to increase with increasing K and decrease with decreasing K If so all factors which may influence the size of K (age *refraction* intraocular pressure hyperemia congestion ocular surgery (*Draeger* 1959 *Ytteborg* 1961)) may also be expected to influence the size of corneal pulse amplitudes

It has previously been shown that retinal detachment surgery is followed by a marked decrease in ocular rigidity (*Syrdalen* 1970b) The present investigation deals with corneal indentation pulse in pre and postoperative retinal detachment eyes in order to evaluate clinically the possible influence a decrease in K will have upon the corneal indentation pulse amplitudes

Material

The present investigation took place during Nov 1968 Aug 1969 The material consists of patients which at the time of examination were hospitalized or had previously been hospitalized in the eye department Rikshospitalet Oslo due to primary retinal detachment in one eye and with a fellow eye without any detachment No eye is included in which there has been a history of ocular trauma glaucoma uveitis or previous ocular surgery (except the actual retinal detachment operation) All patients were examined by the author and all eyes had gonioscopically wide open anterior chamber angles *Preoperative dynamic tonometry* was performed on 34 patients with an average age of 54 3 years (range from 10 to 79 years) In this group 10 patients (25 6 %) were myopic (minus 0 5 or more) and of these 1 (2 6 %) exceeded minus 8 *Postoperative dynamic tonometry* was performed on 39 patients with an average age of 52 9 years (range from 10 to 79 years) In this group 12 patients (30 8 %) were myopic (minus 0 5 or more) and of these 2 (5 1 %) exceeded minus 8 All patients in the postoperative group had been successfully operated for retinal detachment in one eye 28 of these patients had been operated with encircling procedure (cerclage) either alone or in combination with local silicone rubber full thickness scleral implant(s) 10 of the patients had been operated only with local scleral buckling procedure and one patient had been treated with cryo

Table I

Ocular rigidity coefficient (k) in fellow eyes and operated detachment eyes in groups in relation to time after operation. N = number of patients in each group. Numbers in brackets = standard deviation of population.

Method of operation	Interval since operation (days)	N	k fellow eyes	k detach eyes	k fellow − k detach	t value	significance level
Group A Encircling procedures	9–14 (Average = 11)	9	0.0167 (0.0039)	0.0041 (0.0012)	0.0126	9.974	P < 0.001
	19–54 (Average = 3)	9	0.0180 (0.0030)	0.0064 (0.0029)	0.0116	7.187	P < 0.001
	61–10 0 (Average = 257)	24	0.0200 (0.0051)	0.0063 (0.0078)	0.0137	11.414	P < 0.001
	Total (Average = 156)	42	0.0189 (0.0046)	0.0059 (0.0027)	0.0130	16.100	P < 0.001
Group B Local buckling procedures	10–33 (Average = 15)	5	0.0226 (0.0038)	0.0126 (0.0015)	0.0100	5.136	P < 0.01
	69–1 0 (Average = 113)	8	0.0185 (0.0038)	0.0161 (0.0039)	0.0024	3.431	P < 0.02
	Total (Average = 75)	13	0.0201 (0.0012)	0.0147 (0.0036)	0.0054	4.015	P < 0.005

Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

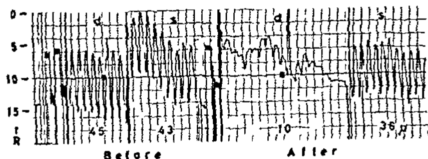


Fig 1
Corneal indentation pulse amplitudes recorded before and after retinal detachment operation (cerclage) right eye d = right eye s = left eye Sensitivity settings 20 mV and ° mV (2 mV = 2 μ per paper division)

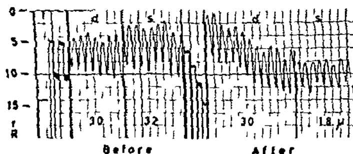


Fig °
Corneal indentation pulse amplitudes recorded before and after retinal detachment operation (local buckling procedure) left eye d = right eye s = left eye Sensitivity settings .0 mV and 2 mV

Comment

Preoperative results In the eyes of the present series corneal indentation pulse amplitudes lower than normal could be expected due to the high incidence of myopia and the possibility of lowered ocular rigidity (*Draeger* 19;9 *Castren* &

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PHOTOCOAGULATION AFTER FANKHAUSER AND LOTMAR

Some clinical experience with a new apparatus

BY

BERTIL LINDER

At the Gonin Club Symposion at Munich in 1966 Fankhauser and Lotmar presented equipment for photocoagulation through the Goldmann three mirror contact glass One apparatus was connected to the ordinary Zeiss photocoagulator working with a xenon lamp as light source Another apparatus operated with a quasi continuous ruby laser developed in the Siemens and Halske laboratories by Ross In 1968 a small series of ten prototypes of a device to be connected to the Zeiss photocoagulator was made in Bern In Lund we were able to buy one of these devices and since September 1968 it has been in frequent use In fact since then the photocoagulator has not been used without this device in cases with peripheric lesions Since no experience with the Fankhauser Lotmar prototype has been presented except in the original articles by the constructors it could be of interest to record our impressions of the device and its use

As described by Fankhauser and Lotmar the apparatus mounted on a corneal microscope table is connected to the arm of the Zeiss photocoagulator (Figs 1 and 2) The only necessary modification to the photocoagulator is to change the original sieve stop for another delivered with the apparatus The new sieve stop can also be used in most cases without the Fankhauser Lotmar device (for further explanation see Fankhauser and Lotmar) With the monocular slit lamp the biomicroscopy and consequently the photocoagulation even of the peripheric part of the fundus through the Goldmann three mirror con

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Table I

Corneal indentation pulse amplitudes (μ) pulsesynchronous change in ocular volum (ΔV mm³) and intraocular pressure in mm Hg Schiotz (P_0) recorded in detachmen eyes and fellow eyes before operation (N = 34) and after operation (N = 39)

		Detachment eyes		Fellow eyes			
		Mean	σ	Mean	σ	t value*	sign level
Preoperative N = 34	μ	24 41	9 156	24 56	9 633	0 168	–
	ΔV	2 375	0 903	2 378	0 937	1 000	–
	P_0	12 26	4 063	13 04	3 088	1 285	–
Post operative N = 39	μ	7 28	6 219	20 72	8 522	10 057	P < 0 001
	ΔV	0 718	0 597	2 032	0 852	10 093	P < 0 001
	P_0	5 75	4 032	14 52	3 124	13 071	P < 0 001
Cerclage N = 28	μ	4 14	3 297	20 64	8 469	12 380	P < 0 001
	ΔV	0 423	0 339	2 02	0 83	12 301	P < 0 001
	P_0	3 8	2 238	14 22	3 423	16 350	P < 0 001
Local procedure N = 11	μ	15 27	4 512	20 91	9 071	3 071	P < 0 02
	ΔV	1 468	0 429	2 064	0 285	2 995	P < 0 02
	P_0	10 7	3 259	15 4	2 221	3 953	P < 0 001

* Statistical method of paired comparison

tested using the method of paired comparison The *preoperative results* show that no difference excists between corneal indentation pulse amplitudes in de tachment eyes and fellow eyes Intraocular pressure is lower in detachment eyes than in fellow eyes but the difference is not statistically significant The *post-operative results* yields a marked difference between detachment eyes and fel low eyes A striking reduction in corneal indentation pulse amplitudes cal culated pulsating ocular volume and intraocular pressure is seen in detachment eyes This reduction is most pronounced in cerclage operated eyes and more moderate in eyes operated with local buckling procedure Fig 1 demonstrates the pre and postoperative recordings from one of the patients operated with cerclage and fig 2 the pre and postoperative recordings from a patient operated with local buckling procedure

special value with the instructive drawings of a rather complete series of classical and effective procedures

Before intraocular intervention for cataract glaucoma in cyclectomy and kerato plasty the author strongly recommends pressure reducing massage of the eye which might be brought about by Vorosmarthy s Oculopressor A rubber pelotte is fixed in front of the eye and insufflated with air Knowing the preoperative intraocular ten sion the manometrically controlled pressure to be withheld in the pelotte during ten minutes necessary for reducing the intraocular tension to 0 5 mm Hg can be read from a diagram The author describes the characteristic effect of this procedure with reduced volume of the vitreous deepening of the anterior chamber etc

This book is recommended *P Brændstrup*

Startup F G Diseases of the Canine Eye Bailliere Tindall & Cassell London 1969 387 pages 272 figures Price £ 6 50

This book is intended primarily for veterinarians who have to treat canine eyes Here and there however there are interesting subjects in which canine pathology differs essentially from human (pathology of the nictitating membrane keratitis with pigmen tations which interfere with vision gonioscopy the motley ophthalmoscopic appearances which make it difficult to recognize abnormalities of the fundus etc)

A more thorough description of a number of ophthalmomedical subjects is missing presumably because present knowledge is deficient

Cataract extraction is described in detail This procedure may be complicated by adhesions between the lens and vitreous an increased tendency to fatal haemorrhage from the iris or the ciliary body capsular rupture and dislocation of the lens Alpha chymotrypsin is recommended in a higher dosage and for a longer period than is customary in human cases

The book is well written and has an ample bibliography and index

M S Norn

Therapie der Augenkrankheiten mit diagnostischen Hinweisen Fibel fur Praxis und Klinik Von Prof R Thiel erganzt von Prof F Hollwich Georg Thieme Stutt gart 1970 XII 527 pp 17 × 24 cm Balacron geb DM 69

This volume contains an enormous amount of concentrated diagnostics and therapy of ocular affections In this way it appears most practically valuable for the engaged ophthalmologist The authors must be highly admired for their ability in precise diag nostic description In the therapeutical directives one again must be impressed by the gains of the last decades presented up to date but also by the vast fields where we lack what looks like a specific therapy and are forced to symptomatic and general pro cedures In this latter category the book also contains many proposals in some of which the reviewer – partly by education – might find himself of a more nihilistic attitude – well knowing that therapy is at the same time an art and a scientific ap proach Sometimes unknown trade marks of drugs cause difficulties

P Brændstrup

mm Hg (local buckling procedure) (*Syrdalen* 1970b) This hypotony in itself would cause only a minor decrease in corneal indentation pulse amplitudes

Conclusions

1 The presence of retinal detachment in an eye will not influence the size of the corneal indentation pulse amplitudes

2 In eyes with a low ocular rigidity the corneal indentation pulse amplitudes will show a corresponding decrease

3 Dynamic tonometry is not a suitable method to measure intraocular pulse synchronous pressure variations (or volume variations) in eyes where ocular rigidity differs in a major degree from normal such as in operated retinal detachment eyes

Summary

The present investigation reports results of dynamic tonometry in 34 patients *with retinal detachment in one eye and with a fellow eye without detachment* Before operation no difference in corneal indentation pulse amplitudes is found between detachment eyes and fellow eyes

Postoperative dynamic tonometry is performed on 39 patients In these detachment eyes a marked reduction in corneal indentation pulse amplitudes (and corresponding pulsating volume of the eyes) is seen The most pronounced reduction is seen in eyes operated with cerclage a more moderate reduction is seen in eyes operated with local buckling procedure The postoperative reduction in ocular rigidity in retinal detachment eyes is considered to be the main reason to the decrease in corneal indentation pulse amplitudes seen with the method of dynamic tonometry

The value of results obtained by dynamic tonometry on paired eyes where ocular rigidity deviates in a major degree from each other is very limited

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Hamburger F A Horror fusionis Bucherei des Augenarztes Vol No 54 F Enke Stuttgart, 1970 Pp VIII + 66 37 figures Price DM 14 00

Again Bucherei des Augenarztes has enriched ophthalmology by a useful monograph this time dealing with one of the clinical recesses Horror fusionis Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of horror fusionis The syndrome of horror fusionis includes according to Hamburger the following elements Persistent diplopia which cannot be corrected by prisms microstrabismus in the form of constant oscillation of the visual axes around zero position apparently normal retinal correspondence abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye.

The book comprises not only the syndrome of horror fusionis but also abnormalities of binocular vision from adjoining fields such as physiological horror fusionis disparity of fixation, microstrabismus aniseikonia, etc The book ends in a postscript by Professor A Linksz in which it is stated int al that the main problem in horror fusionis appears to be horror suppressionis This monograph may be earnestly recommended to readers who take an interest in the problems of binocular vision

E Gregersen

Melvin L. Rubin and Gordon L Walls Fundamentals of Visual Science Charles C Thomas Publisher Springfield Illinois U S A 1969 Pp 435 71 illustrations Price $ 17 50

Presenting the fundamental facts about visual sensory processes in a digestible form to clinical ophthalmologists is no easy job Although more than a hundred years have passed since Helmholtz published his Handbuch der physiologischen Optik and although Marius Tscherning A V Tschermak Seysenegg Francis Heed Adler and Arthur Linksz among others have made efforts to bring physiological optics back to ophthalmology too few modern ophthalmologists are thoroughly familiar with the mechanisms of contrast sensitivity (as a prerequisite to the understanding of visual acuity) dark adaptation colour vision, depth perception, and so forth Melvin Rubin honours as co author his late friend and mentor Gordon L Walls SCD who died in 1967 as professor of physiological optics at the University of California and whose notes of a lecture course make up the basic material of the book

The aim of the present teaching manual is to stress the inspiring as well as clinically important aspects of visual science and in a very didactic manner the author has succeeded in keeping up the reader s interest

The book is divided into four sections

(1) Light and basic concepts
(2) Intensive vision and electrophysiology
(3) Chromatic vision
(4) Spatial vision

Of course the author has not devoted himself equally to all the sections Although the first chapter on the physical properties of light may be understood without much previous knowledge of physics the presentation bears too strong traces of American terminology and measuring units to be easy reading to Scandinavians The chapter on visual acuity does not come up to the presentation of the photochemical basis of vision – and especially not up to that of chromatic vision, a topic on which the author has set his heart judging by his previous publications

Pojola 1962) Within certain limits the corneal indentation pulse amplitudes will increase with increasing intraocular pressure and decrease with decreasing intraocular pressure (*Horven* 1970b) In the present series the average intra ocular pressure both in detachment eyes and in fellow eyes is rather low (as previously seen in other series of retinal detachment patients (*Syrdalen* 1970a b) At this level of intraocular pressure the recorded corneal indentation pulse amplitudes are close to estimated normal values (*Horven* 1970b) The small dif ference in intraocular pressure between detachment eyes and fellow eyes is not expected to induce any larger difference in corneal indentation pulse amplitu des than what demonstrated As there is no significant difference in corneal in dentation pulse amplitudes (or corresponding change in intraocular volume) between detachment eyes and fellow eyes the results indicate that the blood supply in detachment eyes is not different from the blood supply in fellow eyes The presence of retinal detachment in an eye does not induce any change in corneal indentation pulse amplitudes This seems logical if one remembers that the main bulk of blood pumped into the eye during systole goes into the choroid

Postoperative results In the total postoperative group corneal indentation pulse amplitudes in fellow eyes were lower than in preoperatively examined fel low eyes This difference is not statistically significant (Student s t test t = 1 792) and may be caused by difference in materials and the patients getting used to the procedure The postoperative reduction in corneal indentation pulse amplitudes corresponds to postoperative reduction in ocular rigidity previously seen in similar groups of retinal detachment patients (*Syrdalen* 1970b) The present study offers therefore clinical evidence of a close relationship between corneal indentation pulse amplitudes and ocular rigidity The smaller the K value the smaller corneal indentation pulse amplitudes will be recorded

The ΔV values are calculated by use of converting tables depending on data from eyes with presumably normal ocular rigidity The low postoperative ΔV values listed in table I may therefore be fully explained by the low ocular rigidity in these eyes The actual excess of blood pumped into these eyes during systole may as a consequence be of the same order of magnitude as in the fellow eyes According to earlier theoretical considerations (*Syrdalen* 1970b) the cerclage would have to expand only 0 1 mm at each systole in order to increase the ocular volume 2 032 mm³ (postoperative ΔV value of fellow eyes) The pulsating volume of the eye may be the same after operation as before but the method of dynamic tonometry fails in measuring the volume

In the present series intraocular pressure values obtained using Schiotz tono meter and Friedenwald s 1955 table are too low due to the low ocular rigidity The average postoperative intraocular pressure values are therefore quite er roneous Using applanation tonometry the average hypotony of operated de tachment eyes compared to fellow eyes was 2 93 mm Hg (cerclage) and 1 92

As a whole the presentation the superb illustrations and the explanatory analogies in the text classify the author as a trained and enthusiastic tutor and as a master of his extensive subject

The book may be recommended to all ophthalmologists as the most up to date and informative book of its kind

V Dreyer

Dallow R L Television Ophthalmoscopy Charles C Thomas Springfield 1970 Pp XII + 104 $ 8 50

Television ophthalmoscopy means the introduction and application of electronic recording of ocular fundus morphology It is still a relatively untried system in spite of its initiation in 1950 This is certainly due to advances in fundus photography and cinematography over the same period and a consequent preoccupation with the film medium Photography is still superior in the fine resolution of details but television *ophthalmoscopy – besides being a means of teaching –* involves *the possibilities of* electronic processing and quantitation of fundus data These parameters are divided into three categories 1) geometric (static morphologic) data e g diameter of the optic disc and the retinal vessels 2) temporal data e g blood circulation time pulse transmission and retinal artery blood pressure and 3) chromatic data e g evaluation of optic atrophy The book uncovers a future field of automation that well might become of superior importance in fundus studies and necesssary too Should it be possible to present an objective analysis of the diabetic fundus

P Brændstrup

Schlote W Nervus opticus und experimentelles Trauma Beitrag zur Cytologie und Cytopathologie eines zentralnervosen Markfasersystems Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie Vol 131 Editors M Muller H Spatz & P Vogel 156 pages 61 illustrations (Springer Berlin Heidelberg New York 1970)

The experiments were done on the optic nerve of the rat where the uniform system of nerve fibres offers great advantages In addition the extracranial course of the optic nerve between the eyeball and the optic canal permits experimental procedures without damage to other parts of the brain

The author studied the effects of localized trauma of differing intensity to the optic nerve using light and electron microscopy enzyme and histochemistry from 12 hours to 4 months after the injury A distinction is made between three different types of posttraumatic sheath breakdown in the optic nerve The study has been performed with Germanic thoroughness *and the illustrations are excellent*

S Ry Andersen

Sampson Whitney & Gerald L Feldman (ed) Contact Lens Medical Seminar Vol I Charles C Thomas Springfield Illinois 1970 168 pg Price $ 10 50

This is a report of a contact lens seminar held in Palmer House Chicago in connection

Unspecific Shock Therapy in Ophthalmology Symposium Ophthalmologicum Warsaw 15 17 October 1969 Traveaux de la Société de Sciences et des Lettres de Wroclaw Seria B Nr 157 Wroclaw Wroclawska Drukarnia Naukowa. 1969 Pp 255 Price zl 65

The proceedings of the mentioned symposium Part one (19 142) contains the impressive studies of the Warsaw University Eye Clinic of the theoretical and clinical bases of therapy of inflammatory eye diseases with typhoid vaccine and typhoid endotoxin Part two (145 251) consists of papers from other scientific centers dealing with the same subject of nonspecific general stimulation therapy

The classical use and effect of fever therapy are commented by numerous preferably hematologic and serologic studies

In a time with the generally prefered replacement therapy of steroids it is well to recapitulate other effective approaches.

P Brændstrup

Antonin Heinc Das veratzte Auge und die Keratoplastik Bucherei des Augenartzes Heft 52 Ferdinand Enke Stuttgart 1969 91 pages 30 figures 7 tables und 185 references Price DM 20

This book deals with a problem which still awaits its solution The treatment of caustic injuries to the eye The author has given particular attention to lime corrosion and indeed this is reasonable

The introduction is followed by a detailed review of the literature on keratoplasty after caustic injuries The next chapter deals with the treatment and therapeutic results from the Eye Clinic of the palachy University of Olomouc from the period 1948 1964 comprising a total of 46 eyes The presentation of this material is rather cursory and casuistic with many references to previous publications A visual acuity of 5/50 or more was obtained in 21 %

The main emphasis is on a series of experiments on lamellar autotransplantation in 47 rabbits As the main conclusions it is stated that a lamellar graft may heal in a cornea with fresh lime corrosion and that the earlier the grafting is done the more favourable is its result On this basis the author advises a chaud lamellar keratoplasty in cases of human lime corrosions

Niels Ehlers

Jaffe Norman S The Vitreous in Clinical Ophthalmology 310 pages, 334 figures including 11 in colour C V Mosby Comp St. Louis 1969 Price $ 32.50

The author is assistant professor to the University of Miami School of Medicine and teacher at the Academy of Ophthalmology courses on the vitreous body

The book deals with subjects such as the embryology anatomy ultrastructure, and biochemistry of the vitreous systematic slit lamp examination the ascension phenomenon the condition of the anterior hyaloid membrane after cataract extraction (holes, prolapse vitreous strings) collapse of the vitreous mentioning Linder's thesis the role of the vitreous in retinal detachment in diabetes, in pupillary block, etc.

O A Jensen's studies on primary hyperplastic persisting vitreous are quoted. The

with the October 1968 meeting of the American Academy of Ophthalm and Otolaryng Similar seminars are to be held every other year and to be published in the same way This volume appeared 18 months after the meeting was held

At the seminar practical aspects were in the forground There are chapters on the *prescription of* contact lens with topogokeratometer on modification and finishing of contact lenses follow up on patients wearing contact lenses wearing time and on special problems such as aphakia keratoconus and postkeratoplasty states on toric lenses on the selection of patients with motor anomalies for contact lenses

In a chapter on flush fitting lenses as a therapeutic measure in bullous keratitis corrosion, pemphigus etc it is established that these are highly specialized tasks which should be restricted to hospitals and which require int al a fulltime technician.

The book closes with a report of a lively panel discussion Great importance is attached to diagnosing incipient corneal oedema as soon as possible i e by scleral scatter without magnification.

Reduced or insufficient blinking may give rise to trouble and shorten the wearing time the anterior surface of the contact lens may be dry These patients should be instructed in forced blinking e g for 10–15 minutes in the event of incipient burning or dimming

Soft lenses are criticized but possibly have a special indication e g instead of flush fitting lenses a matter which may be of interest when Bausch & Lombs lenses appear on the market

There are discussions concerning fenestration of minicontact lenses bifocal lenses on front toric back toric and bitoric lenses on dry spots and on Schirmer s test

The book is readable and worth recommending to all who take an interest in contact lens problems

M S Vorn

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VARIA

European Ophthalmic Pathology Society

Held its ninth annual meeting in Ghent Belgium from 28th 30th May 1970 Dr F C Blodi (Iowa City U S A) and Professor J François (Ghent) were the guests of honour Invited guests were Dr E Balestrazzi (Italy) and Prof M Brihaye van Geertruyden (Belgium) The meeting was attended by 31 members The next meeting will be a Joint Meeting with the American Verhoeff Society which is celebrating its 25th anniversery and will be held in London on the 25th to 28th April 1971 Prof N Ashton will act as organising secretary

The XX Nordic Ophthalmological meeting

will be held in Reykjavik on June 23rd to 26th 1971

1 The intraocular pressure

2 Diabetes mellitus and the Eye

There will be an opportunity to read papers other than those on the main subjects Further informations concerning announcements hotelbookings etc. will be given out at a later date

Any inquires can be directed to Augnlæknafélag Islands (Icelandic Ophthalmological Society) box 954 Reykjavik

increase of cornea and lenticular power and possibly also an unrelated decrease of axial length occurs in young people after the age of 14 Sex differences were not obvious and bodily length and weight without relationship

Our knowledge of dynamics of the infantile eye below 3 years of life is still poor The concept of Emmetropization is considered outmoded

P Brændstrup

Recent Research on the Retina British Medical Bulletin vol 26 No 2 *Brit Council* London. May 19 0

Our readers attention are drawn to this volume of British Medical Bulletin. Prof N Ashton acted as Chairman of the committee that planed this number and Prof E. S Perkins as scientific editor The volume contains 17 chapters on recent advances in retinal research Most of the work are British and the authors of high esteem

H Ehlers

Keeney Arthur H (editor) *Proceedings of the Eleventh Annual Meeting of the American Association for Automotive Medicine.* C. C. Thomas Springfield Illinois 19 0 ?98 pages *including index and illustrations Price* $ 19 75

Traffic accidents and traffic medicine are gaining ever increasing importance in industrialized society This has int. al given rise to the foundation of The American Association for Automotive Medicine which has now existed for 10 years and on this occasion has published the present monograph

The book comprises ?3 chapters dealing with widely different subjects related to traffic injuries and traffic safety (alcohol, analysis of accident materials psychological factors driving research) medical aspects in driver licensing attacks of d ea e with loss of consciousness during driving prophylactic measures such as teaching propaganda and safety helmets etc)

Chapters of more specific ophthalmological interest are e g Drug induced Disturbances of Vision that May Affect Driving (W Morton Grant) Ocular Findings in Extension flexion Injuries of the Cervical Spine (William J Gibson) and Some Relationships between Vision and Driving (Albert Burg) In this last mentioned chapter emphasis is laid on the requirement for developing a cheap and compact apparatus for testing dynamic vision and a well su ted equipment for testing night vision (threshold and glare recovery measurements)

The book may be recommended to the ever increasing number of doctors and other special sts who are being involved in the different aspects of traffic medicine.

E Gregersen

Blakovics Kettesy *Augenärztliche Operationslehre* (?) E ngriffe am Auge. 4 edit. by *D Vorosmarthy* Enke Stuttgart. 19 0 VII 450 pp 5 1 figs DM 107

The three former editions of this ocular surgery appeared in 1935 1945 and 1959 This fourth edition has been thoroughly revised by Vorosmarthy but its general character of a handy precise, well selected presentation has remained.

The chapter dealing with surgery of the eyelids (115 pages) has always been of

(From the Ophthalmological Department
Central Hospital Næstved (Head Viggo Clemmesen M D)
and The Umanaq Health Service (Medical Officer P H Alsbirk)

PRIMARY GLAUCOMA IN GREENLAND
(Umanaq District)
I Introduction The Normal Intraocular Pressure

BY

P H ALSBIRK

The epidemiology of the main types of glaucoma is being studied in many countries during the present years Complete understanding of the genetic and other etiologic factors on which it depends is slowly approaching The two major types of primary glaucoma are open angle glaucoma (o a g) and angle closure glaucoma (a c g) The former disease is a prominent cause of blindness in Europe America and Africa, where it occurs more frequently than angle closure glaucoma Among the Mongoloids of Asia glaucoma seems to be infrequent our scattered knowledge within this field suggests however that angle closure glaucoma is the more frequent of the two forms This appears for instance from studies made in Burma (a c g/o a g rate 330/25) and in Thailand and among Chinese from Hong Kong and Singapore (*Ida Mann* 1966 *Loh* 1968) Mann s geographic studies suggest as does clinical experience that the two types of glaucoma are separate disease entities depending in particular on genetic factors which seem to be unevenly distributed throughout the world However systematic surveys of populations outside Europe and the U S A which might further illustrate the global pattern would be highly desirable.

The arctic zones of the earth are inhabited by small groups of people who through innumerable generations have lived in total or relative isolation – and

Received October 29th 1969

classification into cases occurring at an early stage of gestation and entailing multiple defects (microphthalmos iridic coloboma glaucoma retinal dysplasia) as distinguished from late cases which are uncomplicated is emphasized as being of great value

Bleeding into the various sites and spaces of the vitreous is mentioned and the prognosis of the various forms of bleeding is tentatively set up

Central effusion in the macular area and vitreous traction in the posterior pole inherited diseases of the vitreous (Wagner s degeneration (defect in the primordium of the secondary vitreous body Goldman Favre s degeneration and hereditary juve nile retinoschisis) are discussed

Amyloidosis is reviewed general as well as localized in the vitreous The few but interesting attempts at exchanging the vitreous are reported

Under the heading of vitreous surgery the author also mentions the very advanced technique of cutting membranes and deep adhesions as well as vitreous transfer and vitreous replacement

He emphasizes the role of the vitreous body in cataract extraction If loss of vitreous has occurred he recommends bending the cornea and removing all the vitreous tissue remaining in the anterior chamber by means of cellulose sponges so that the iris re tracts and the vitreous is left at or behind the pupillary level

In postoperative corneal oedema caused by vitreous strings which do not yield to pupillary dilatation and osmotic treatment the author recommends removal of all vitreous tissue from the anterior chamber This is done by sclerotomy and an open sky procedure using the above mentioned cellulose sponges

To reduce the volume of the vitreous body during cataract extraction the author ad ministers glycerol 90 g by mouth 90 minutes prior to the operation This shrinks the vitreous and reduces the risk of loss or prolapse of the vitreous body No major side effects are said to have occurred in the author s 1500 cases

This book affords an admirable didactic presentation of the subject with a clear classification good illustrations and up to date references It may be recommended as an excellent modern description of problems relating to the vitreous body

M S Norn

Sorsby A & G A Leary A longitudinal study of refraction and its components during growth Medical Research Council S R S 309 London Her Majesty s Stationa ry Office 1970 Pp 41 Price 9s 0d (45p) net

The present study should be read as a supplement to the Council s series No 301 and 293 Professor Sorsby and his colleagues in a cross sectional study of 1400 children between the ages of 3 and 15 presented the evidence that the optical components of the eye do not vary freely but are correlated so that high powers of the cornea and lens go with short axes and low powers with long axes A considerable range of axial length may be accompanied by emmetropia provided complete correlation Incomplete correlation accounts for all spherical errors except high hypermetropia and high myo pia usually determined by axial length

In the actual study 129 of the original children were further followed up The rapid growth of the infantile eye is followed by a gradual slowing untill puberty In 75 % axis length increase 1 to 1 5 mm considered normal while in 25 % a higher anomal ous increase is seen Anomalous elongation is not counteracted by a corresponding reduction of cornea and lenticular power and plays a considerable role in reduction of high hypermetropia and development of myopia It has been observed that paradoxical

under conditions as regards light and temperature which differ greatly from the physical environments of the more densely populated parts of the earth

In northern parts of the USSR glaucoma is the most frequent cause of blindness (in 35 per cent of the blind) The cases are often severe with a painful course The number of persons consulting doctors increase greatly during the dark and cold period of the year Acute glaucoma accounts for about 19 per cent of the cases (*Baljasnikova* 1963) No mention is made of gonioscopic findings

In Iceland glaucoma is the cause of blindness in 60 per cent of the blind who in 1950 were 3 per thousand of the population (*Bjornsson* 1967) Through a 25 year period *Sveinsson* (1959) examined 1544 glaucoma patients of whom 90 per cent suffered from glaucoma simplex and less than 2 per cent from acute glaucoma Two thirds of the patients were men Predisposition to glaucoma and/or blindness was found in almost half of the cases Among 237 patients with primary glaucoma Bjornsson found by gonioscopy 6 per cent with angle closure glaucoma and only 2 1 per cent who had shown actual attacks

As regards the *Eskimo* populations our knowledge is limited According to Ida Mann glaucoma is rare most frequently of the narrow angle type as among the Mongoloids In 1968 Speakman found among 200 adult Eskimos in Canada three with angle closure glaucoma and two with pronounced chronical glaucoma

Earlier observations with regard to glaucoma in *Greenland* was summarized by Bertelsen in his large nosography (1940a) Primary glaucoma has been mentioned as early as 1909 and is said to occur relatively frequently both in northern and southern districts and to be an important cause of blindness (*Norman-Hansen* 1911 *Borresen* 1926 *Hertz* 1929 *Skeller* 1949)

Blindness is much more frequent in Greenland than in other parts of Denmark in 1937 it was thus ten times as frequent in the population groups above 16 years of age During the years 1910 1929 the frequency of blindness was 3 per thousand with leucomas and glaucoma as the most frequent causes (*Bertelsen* 1940b) In 1962 the ophthalmologists Clemmesen and Skydsgaard studied the prevalence of blindness on Greenland s west coast and found it to be 2 5 per thousand (*Skydsgaard* 1963) Among 69 blind persons 44 were blind from primary or secondary glaucoma 39 of them with vision of 1/60 or less Of those who were blind due to glaucoma almost 80 per cent were women In the latest statistics – from 1968 – the prevalence of blindness was found to be 3 per thousand (*Clemmesen* 1969)

By way of comparison mention may be made of the latest survey made in Denmark and comprising the island of Falster It is based on the same blindness criteria (visual acuity $\leq$ 4/60) and covers a population slightly larger than that of Greenland Here *Norskov* (1968) found a blindness prevalence of 1 24 per thousand likewise with primary glaucoma as the most frequent cause (in 29

Hamburger F A Horror fusionis Bucherei des Augenarztes Vol No 54 F Enke Stuttgart 1970 Pp VIII + 66 37 figures Price DM 14 00

Again *Bucherei des Augenarztes* has enriched ophthalmology by a useful monograph, this time dealing with one of the clinical recesses Horror fusionis Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of horror fusionis The syndrome of horror fusionis includes according to Hamburger the following elements Persistent diplopia which cannot be corrected by prisms microstrabismus in the form of constant oscillation of the 2 visual axes around zero position apparently normal retinal correspondence abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye

The book comprises not only the syndrome of horror fusionis but also abnormalities of binocular vision from adjoining fields such as physiological horror fusionis disparity of fixation, microstrabismus aniseikonia etc The book ends in a postscript by Professor A Linksz in which it is stated int. al that the main problem in horror fusionis appears to be horror suppressionis This monograph may be earnestly recommended to readers who take an interest in the problems of binocular vision

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per cent) As regards the whole of Denmark the blindness prevalence is generally stated to be 0 75 1 per thousand

The part played by glaucomatous diseases in the great problem of blindness in Greenland is thus of such significance as to motivate a more intensive study of a larger group of the population The main object of such a population study would be to throw light upon the prevalence and types of glaucomatous diseases in the district However fundamental epidemiological knowledge within this field might serve as a valuable basis for intensified diagnostic terapeutic and prophylactic efforts throughout the whole of Greenland and probably have more general significance

Glaucoma Survey in the Umanaq District in 1967

1) Geography Population and Health Service

Umanaq district is situated on the west coast of Greenland in about 71° northern latitude the same latitude as the North Cape of Norway In this district the dark period of the year lasts from the beginning of November to the beginning of February and during a corresponding period of the summer the sun does not set The population is Eskimoic with a certain admixture of Caucasian blood On December 31 1966 it numbered altogether 2289 persons The main town of the district Umanaq which is situated on a small island has a population of 934 of which 844 are Greenlanders The remaining population in the district – 1345 Greenlanders and 10 non Greenlanders – lives in eight villages at distances of from 21 to 123 kilometres from the town Medical service is provided by two doctors two to three nurses and a midwife who are stationed in the town but who are on frequent tours or called out to the villages whenever the sea is navigable or the ice safe for dog sledge transport. During several weeks annually – before and after the sledge season – it is impossible for people living in the villages to consult a doctor Each village is attended by a native part trained midwife who has been given an education including nursing and first aid for three to four years at a local hospital However her theoretical knowledge – also with regard to eye diseases – is very limited She has a comprehensive store of medical agents comprising medicaments for the management of glaucoma Wireless connection from the villages to the town was established as late as 1968 Different ophthalmologists visit the district every or every second year for a few days but the time at their disposal is sufficient only for superficial examinations and the standard equipment available does not allow for the performance of biomicroscopy gonioscopy or applanation tonometry For the remaining part of the year ophthalmological problems must be looked after to the best of their ability by doctors without

special value with the instructive drawings of a rather complete series of classical and effective procedures

Before intraocular intervention for cataract glaucoma in cyclectomy and kerato plasty the author strongly recommends pressure reducing massage of the eye which might be brought about by Vorosmarthy s Oculopressor A rubber pelotte is fixed in front of the eye and insufflated with air Knowing the preoperative intraocular ten sion the manometrically controlled pressure to be withheld in the pelotte during ten minutes necessary for reducing the intraocular tension to 0 5 mm Hg can be read from a diagram The author describes the characteristic effect of this procedure with reduced volume of the vitreous deepening of the anterior chamber etc

This book is recommended *P Brændstrup*

Startup F G Diseases of the Canine Eye Bailliere Tindall & Cassell London 1969 387 pages 272 figures Price £ 6 50

This book is intended primarily for veterinarians who have to treat canine eyes Here and there however there are interesting subjects in which canine pathology differs essentially from human (pathology of the nictitating membrane keratitis with pigmen tations which interfere with vision gonioscopy the motley ophthalmoscopic appearances which make it difficult to recognize abnormalities of the fundus etc)

A more thorough description of a number of ophthalmomedical subjects is missing presumably because present knowledge is deficient

Cataract extraction is described in detail This procedure may be complicated by adhesions between the lens and vitreous an increased tendency to fatal haemorrhage from the iris or the ciliary body capsular rupture and dislocation of the lens Alpha chymotrypsin is recommended in a higher dosage and for a longer period than is customary in human cases

The book is well written and has an ample bibliography and index

M S Norn

Therapie der Augenkrankheiten mit diagnostischen Hinweisen Fibel fur Praxis und Klinik Von Prof R Thiel erganzt von Prof F Hollwich Georg Thieme Stutt gart 1970 XII 527 pp 17 × 24 cm Balacron geb DM 69

This volume contains an enormous amount of concentrated diagnostics and therapy of ocular affections In this way it appears most practically valuable for the engaged ophthalmologist The authors must be highly admired for their ability in precise diag nostic description In the therapeutical directives one again must be impressed by the gains of the last decades presented up to date but also by the vast fields where we lack what looks like a specific therapy and are forced to symptomatic and general pro cedures In this latter category the book also contains many proposals in some of which the reviewer – partly by education – might find himself of a more nihilistic attitude – well knowing that therapy is at the same time an art and a scientific ap proach Sometimes unknown trade marks of drugs cause difficulties

P Brændstrup

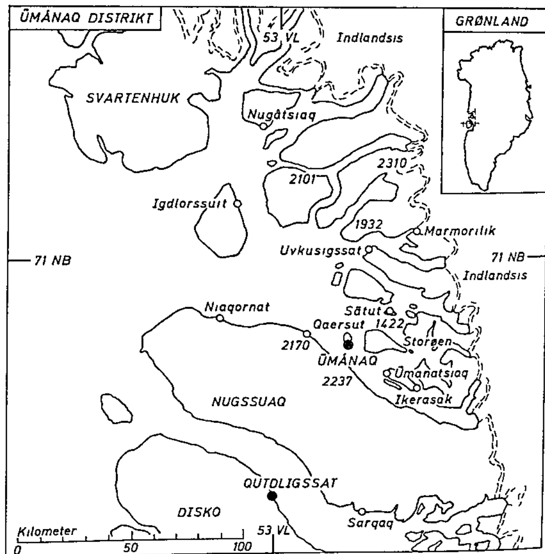


Fig 1
(Map of Umanaq district)
The complex of islands peninsulas and ice fiords of the Umanaq bay The town and the eight villages are scattered over an area of about the same magnitude as Kattegat The neighbouring districts are to the north Upernavik and to the south Qutdligssat and Jakobshavn

ophthalmological training *Alsbirk & Schioler* (1969) have given a description of the medical work and the morbidity in the district

2) Preliminary Glaucoma Occurrences

During the period 1964 1966 nine attacks of intermittent and acute glaucoma

Hamburger F A Horror fusionis Bücherei des Augenarztes Vol No 54 F Enke Stuttgart 1970 Pp VIII + 66 37 figures Price DM 14 00

Again Bücherei des Augenarztes has enriched ophthalmology by a useful monograph this time dealing with one of the clinical recesses Horror fusionis Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of horror fusionis The syndrome of horror fusionis includes according to Hamburger the following elements Persistent diplopia which cannot be corrected by prisms microstrabismus in the form of constant oscillation of the 2 visual axes around zero position, apparently normal retinal correspondence abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye

The book comprises not only the syndrome of horror fusionis but also abnormalities of binocular vision from adjoining fields such as physiological horror fusionis disparity of fixation, microstrabismus aniseikonia, etc The book ends in a postscript by Professor A Linksz in which it is stated int al that the main problem in horror fusionis appears to be horror suppressionis This monograph may be earnestly recommended to readers who take an interest in the problems of binocular vision

E Gregersen

Melvin L Rubin and Gordon L Walls Fundamentals of Visual Science Charles C. Thomas Publisher Springfield Illinois U S A 1969 Pp 435 71 illustrations Price $ 17 50

Presenting the fundamental facts about visual sensory processes in a digestible form to clinical ophthalmologists is no easy job Although more than a hundred years have passed since Helmholtz published his Handbuch der physiologischen Optik and although Marius Tscherning A V Tschermak Seysenegg Francis Heed Adler and Arthur Linksz among others have made efforts to bring physiological optics back to ophthalmology too few modern ophthalmologists are thoroughly familiar with the mechanisms of contrast sensitivity (as a prerequisite to the understanding of visual acuity) dark adaptation colour vision, depth perception and so forth Melvin Rubin honours as co author his late friend and mentor Gordon L Walls SCD who died in 196 as professor of physiological optics at the University of California and whose notes of a lecture course make up the basic material of the book

The aim of the present teaching manual is to stress the inspiring as well as clinically important aspects of visual science and in a very didactic manner the author has succeeded in keeping up the reader s interest

The book is divided into four sections

(1) Light and basic concepts
(2) Intensive vision and electrophysiology
(3) Chromatic vision.
(4) Spatial vision

Of course the author has not devoted himself equally to all the sections Although the first chapter on the physical properties of light may be understood without much previous knowledge of physics the presentation bears too strong traces of American terminology and measuring units to be easy reading to Scandinavians The chapter on visual acuity does not come up to the presentation of the photochemical basis of vision – and especially not up to that of chromatic vision a topic on which the author has set his heart, judging by his previous publications.

were detected and treated The patients were seven women from 46 to 63 years of age without any earlier history of glaucoma Two of the cases were so severe that vision was lost on the eye in question the others were successfully controlled by medical treatment One man with poor vision and three women who on account of glaucoma attacks were without perception of light died during this period From before 1964 another two cases were known of women without perception of light in one and both eyes respectively due to typical glaucoma attacks

This accumulation of glaucoma attacks in such a small population comprising just under 200 women above the age of forty was the direct inspiration and basis of the present study

3) Method

Systematic glaucoma surveys of larger groups of the population in Greenland have not been published previously and the available papers do not enable any classification of the glaucoma cases according to gonioscopic findings As mentioned clinical experience suggested a considerable incidence of angle closure glaucoma in Umanaq district

It could hardly be expected that it would be possible by tonometric methods to detect a c g cases in the interparoxysmal periods It was nevertheless decided primarily to perform a tonometric screening in order to determine the tension level of normal eyes the extent to which ocular hypertension occurs and to detect unknown cases of o a g and advanced cases of a c g Secondarily it was planned to extend the examination programme to comprise methods which were more adequate for the detection of a c g cases also at earlier stages

Tonometric anamnestic screening was therefore performed as follows the national register for the district was gone through systematically and punch cards written out for all Greenlanders who on January 31 1966 had attained the age of twenty in the town and forty in the villages The register had just been carried up to date with this date as terminal date

People were invited to attend the examination by a letter in Greenlandic in which a brief description of the object of the examination and of the procedure was given In the town the examination took place in a ward in the hospital and in the villages in the school room Two beds or two couches consisting of desks with rugs were placed with the heads immediately below a red disk in the ceiling Each person was present during the examination of his predecessor to reassure and to make the procedure clear Persons to be examined were made to rest on the couch for exactly five minutes to calm down before tonometry was performed All examinations were made by the author assisted by an interpreter and in most cases by a nurse

The following observations were made in the order named

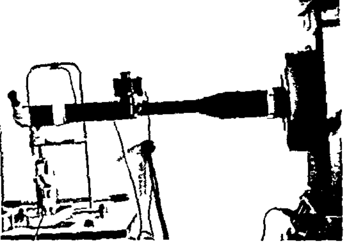


Fig 1
Front view of the Fankhauser Lotmar device connected to the Zeiss photocoagulator

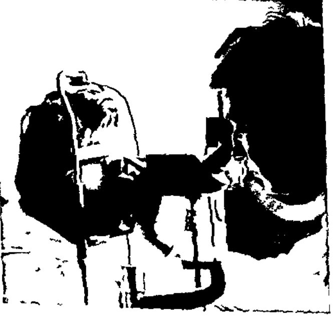


Fig 2
Side view

From the University Eye Clinic Lund Sweden
(Head Professor Erik Palm M D)

PHOTOCOAGULATION AFTER FANKHAUSER AND LOTMAR

Some clinical experience with a new apparatus

BY

BERTIL LINDER

At the Gonin Club Symposion at Munich in 1966 Fankhauser and Lotmar presented equipment for photocoagulation through the Goldmann three mirror contact glass One apparatus was connected to the ordinary Zeiss photocoagulator, working with a xenon lamp as light source Another apparatus operated with a quasi continuous ruby laser developed in the Siemens and Halske laboratories by Ross In 1968 a small series of ten prototypes of a device to be connected to the Zeiss photocoagulator was made in Bern In Lund we were able to buy one of these devices and since September 1968 it has been in frequent use In fact since then the photocoagulator has not been used without this device in cases with peripheric lesions Since no experience with the Fankhauser Lotmar prototype has been presented except in the original articles by the constructors it could be of interest to record our impressions of the device and its use

As described by Fankhauser and Lotmar the apparatus mounted on a corneal microscope table is connected to the arm of the Zeiss photocoagulator (Figs 1 and 2) The only necessary modification to the photocoagulator is to change the original sieve stop for another delivered with the apparatus The new sieve stop can also be used in most cases without the Fankhauser Lotmar device (for further explanation see Fankhauser and Lotmar) With the monocular slit lamp the biomicroscopy and consequently the photocoagulation even of the peripheric part of the fundus through the Goldmann three mirror con

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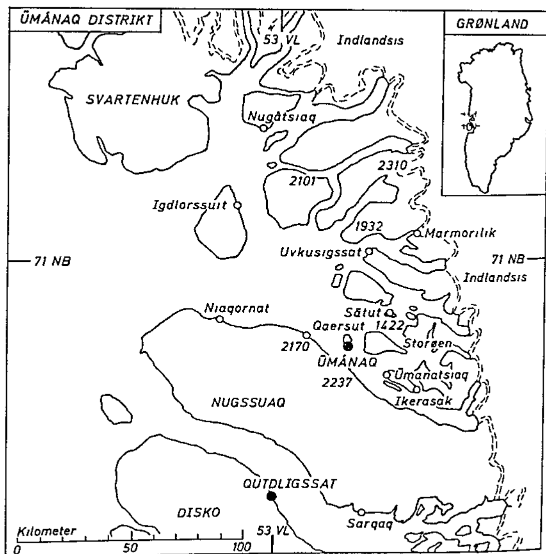


Fig 1

(Map of Umanaq district)

The complex of islands peninsulas and ice fiords of the Umanaq bay The town and the eight villages are scattered over an area of about the same magnitude as Kattegat The neighbouring districts are to the north Upernavik and to the south Qutdligssat and Jakobshavn

ophthalmological training *Alsbirk & Schioler* (1969) have given a description of the medical work and the morbidity in the district

2) Preliminary Glaucoma Occurrences

During the period 1964 1966 nine attacks of intermittent and acute glaucoma

very little in comparisons of the results from town and villages with respect to the age group above forty

The fact that the town population was examined between 16 and 18 o clock and the villagers at different times does however tend to diminish the possibility of ascertaining any possible small differences because due to physiological diurnal variations in the intraocular pressure the highest values will obtain in the morning and the lowest in the evening (*Katavisto* 1964)

The mean tension of the normal eye in Greenlanders has thus been found to be 15 7 mm Hg (corresponding to a scale reading of 8 with 7 5 g weight on the Schiotz tonometer) and a standard deviation of 3 0 mm Hg

Discussion

For epidemiological surveys of the prevalence of glaucoma and the normal ocular tension in large population groups Schiotz tonometry has been used extensively until recently Table III lists the results of a number of such surveys which compared to the findings from Umanaq district show that normal eyes in Greenlanders do not on the whole differ from American German Finnish Norwegian or British eyes *Leydhecker et al* (1958) found no difference between right and left eyes or sexes while *Katavisto & Sammalkivi* (1964) and *Hollows & Graham* (1965) found significantly higher tensions in women than in men –

Table III
Schiotz tonometry applied to normal eyes
(according to Friedenwald s calibration 1955)

	Number of eyes	Mean tension mm Hg	Standard dev mm Hg
Becker 1958	909	16 1	2 80
Leydhecker et al 1958	19 880	15 5	2 57
Katavisto & Sammalkivi 1963	11 520	16 00	2 72
Bertelsen T et al 1965	3812	14 8	2 7
Hollows & Graham 1965			
men left eye Schiotz	1914	14 6	2 96
men left eye applanation	1873	(15 9)	(2 87)
women left eye Schiotz	2258	15 7	2 87
women left eye applanation	2169	(16 6)	(2 88)
Alsbirk 1967	1108	15 7	3 0

examined in bright daylight – to maintain the same examination times in town and villages was impossible for practical reasons

4) Material

The population groups examined comprised as mentioned all Greenlanders in the town of Umanaq who had attained twenty years of age and all in the vil lages who had attained the age of forty

Table I gives the distribution of the subjects according to age sex and place of residence the sex distribution is almost equal Fig 2 shows how relatively young the population is The age group 20 39 amounts to 23 9 per cent of the population – almost as in the rest of Denmark – but in Umanaq district there are only 18 5 per cent who are more than forty years of age – as against 41 5 per cent in the rest of Denmark On the whole the age distribution is the same as in the whole of Greenland

Before the completion of the survey there was a small diminution in numbers due to deaths and removals to other districts There were six inhabitants in the district whom we did not succeed in getting hold of because they were away fishing or working in the mines or were not interested in cooperation Only one – an old paranoic psychotic woman – refused categorically to be examined

Table I

Person examined in Umanaq district 19[illegible]7

Age	Town		Villages		Whole district		Total
	♂	♀	♂	♀	♂	♀	♂ + ♀
0– 9	39	47	–	–	39	47	86
30–39	41	61	–	–	41	61	102
0–39	80	108	–	–	80	108	188
40–49	32	17	41	47	73	64	137
0–59	91	[illegible]9	49	35	0	64	134
60–69	1[illegible]	16	35	34	47	50	97
0– 9	5	5	7	5	12	10	22
80+	1	1	1	3	2	4	6
40–80+	71	68	133	1[illegible]4	204	19[illegible]	396
0–80+	151	1[illegible]6	133	1[illegible]4	284	300	584

in the Finnish survey particularly in the age groups 50 59 and 60 69 years In the latter study a significant difference was also observed between right and left eyes with a slightly higher tension in left eyes

Results obtained by means of Goldmann s applanation tonometer are more reliable and better comparable than those from a weight tonometer as the Schiotz tonometer Comprehensive analyses of the influence of age and sex using applanation tonometry have confirmed that in the age group above forty the intraocular pressure is higher in women than in men (*Armaly* 1965 *Hollows & Graham*) and further that it increases with age most markedly in women (Armaly) The latter author considers the results to be related to the hormonal changes of the menopause He found moreover the standard deviations to increase significantly with age equally much in both sexes

Since Leydhecker s tonometric screening of 10 000 persons deviations from the Gaussian curve on high tension levels have played a great part in glaucoma discussions *Leydhecker et al* (1958) showed the distribution to consist of a minor partial collective in the high tension range – in his view representing incipient pathological cases – and a major main collective accurately accounted for by the Gaussian distribution curve

The sharp assessment of suspect and definitely pathological tension values at $\bar{x} + 2s$ and $\bar{x} + 3s$ respectively has been strongly criticized however and the discussion is still going on compare for instance the Tutzing Castle Symposium 1966 and *Pollack* (1968)

Davanger (1965) considers persons with both intraocular hypertension and simple glaucoma to represent purely quantitative extremes in the high tension range consequent upon the physiological increasing resistance in the porous system of the trabecular meshwork which occurs with age With normal distribution of effective pore diameters in the population it will be seen by applying simple flow physiological laws to the problem that the same constriction of the pores for instance 5 per cent will result in a higher increase in tension on a high pressure level than on a low pressure level According to Davanger the skewness to the right is thus an expression of an actual deviation from the Gaussian distribution secondary to the normally distributed pore diameters

According to Armaly s and Hollow & Graham s thorough surveys of representative samples the distribution is still skew to the right with preponderance on the high tension levels but it has also been shown that viewed separately within the individual age and sex groups the distribution seems normal It is only when the age is above sixty that a significant preponderance of high values will be found

The population group with which the present study is concerned is too small to allow such detailed analyses There is however no marked skewness to the right in the curves of fig 4 Even when the values for both sexes and both eyes are combined in one curve fig 5 the conclusion must be that this material does

a) Classification of the *physiognomy* of the person examined as being Eskimoic" or "mixed" when judged at a distance before the colour of the eyes could be seen

b) Observation of the *colour of the iris* which was recorded as being either "pure brown" or "mixed"

c) Recording of such abnormalities in the *anterior segment* of the eye as were immediately visible in strong light (diseases of the cornea or iris or their sequelae besides obvious cases of cataract)

d) Determination of the intraocular pressure (right eye first) by means of a *tension indicator according to the applanation principle* designed by *Bruun Jensen* (1967) after anaesthesia and staining of the tear fluid with fluorescein The tension was determined as being above equal to, or lower than 21 mm Hg

e) *Measurement of the* intraocular pressure with a *Schiotz tonometer* (Riester No 4820) adjusted and controlled on Sept 18 1966 at the Danish tonometer centre and found by micrometric control to be in order after the completion of the screening A 7 5 g weight was applied and the mean value of the first few oscillations expressed to the nearest whole or half scale unit was recorded For one day s measurements in one of the villages it became necessary to use another Schiotz tonometer but subsequent micrometric control showed this instrument to be correct and in full agreement with the former one

As regards relations between scale units and intraocular pressures in mm Hg Friedenwald s calibration (1955) was used

f) When the measurements were completed the person was asked whether there were *blind persons in his family* either among parents grandparents or other relatives

g) The person examined was intervized as to *previous serious eye diseases* Only information which was relevant in connection with items c) d) and e) was recorded however

h) The person was asked whether *ophthalmological examination had been performed previously* (all ophthalmological case records were subsequently studied with a special view to previous tension determinations)

i) By means of a flash light and *a halo-viewer* (from Campbell Pharmaceuticals Inc) rainbow rings around a source of light were demonstrated The interpreter asked the following question uniformly of everybody Have you seen such coloured rings round light when you have suffered from a headache? On an affirmative reply more detailed data with regard to such cases were recorded

On account of transport problems and for other reasons the people in the town were all examined during the months of January February and the beginning of March and the inhabitants of the villages during May June and July The people living in the town were thus all examined during the afternoon darkness (from 16 to 18 o clock) while those in the villages were always

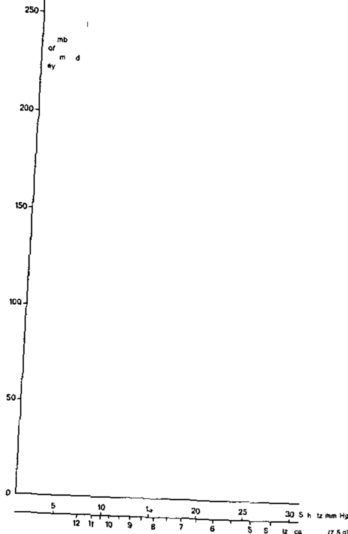


Fig 5

Intraocular pressure of normal eyes Distribution curve for 1108 eyes without reference to right or left eyes or sex The curve has a smooth course through whole and half *tonometer scale* units and illustrates the absence of skewness to the right

not show any skewness to the right on high tension levels It should be pointed out, however that 78 6 per cent of the persons examined were under sixty years of age

Correct sampling of the subjects to be used for studies of normal physiological conditions as the intraocular pressure is of fundamental importance Healthy people in their usual environments are better probands than for instance patients in non ophthalmological departments – who have frequently been used (example Katavisto & Sammalkivi) The Umanaq survey is a total population study as regards the age groups above forty and in the case of the town popu

examined in bright daylight – to maintain the same examination times in town and villages was impossible for practical reasons

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Table I
Persons examined in Umanaq district 1967

Age	Town ♂	Town ♀	Villages ♂	Villages ♀	Whole district ♂	Whole district ♀	Total ♂ + ♀
20—29	39	47	—	—	39	47	86
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40—49	32	17	41	47	73	64	137
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70—79	5	5	7	5	12	10	22
80+	1	1	1	3	2	4	6
40—80+	71	68	133	124	204	192	396
20—80+	151	176	133	124	284	300	584

lation the groups above twenty years of age The time at disposal did not allow for the inclusion in the study of the group from 20 to 39 years of age in the villages It was considered however that the numbers of this age group in Umanaq town were high enough for the purpose

The delimitation of what may be described as normal" in such a population is always difficult In this case it was decided to neglect the frequently variegated descriptions of diseases and symptoms with which a suggestible and eye minded population would often reply to questions about previous severe eye diseases Of eyes with thin corneal maculae forty were included Since their tension was found to be distributed evenly about a mean value of 15 2 mm, i e almost equal to and at any rate not above the total average of 15 7 mm they were not excluded

Schiøt tonometers are delicate instruments of limited precision *Schwartz & Ambler* (1964) have convincingly demonstrated the errors in adjustment which could be found in five new certified tonometers In 700 duplicate measurements applying all possible combinations it was found that the difference between the results obtained by means of the two tonometers which differed most from each other was on an average as much as 0 55 scale units This corresponds to 1 4 mm Hg in the medium range and 2 0 in the important upper range Consequently too much weight should not be attached to minor differences in the mean values obtained from different samples and the same applies to the values $\bar{x}$ + 2s and $\bar{x}$ + 3s But it does *not* invalidate the demonstration that differences exist between comparable sub groups in a sample as the present

The weight used throughout the present study was 7 5 g It was chosen especially because a weight of 5 5 g would necessitate a more frequent change to a heavier weight – at scale unit 4 and lower values (*Becker & Schaffer* 1965) Such a change over may introduce a spurious bimodality as shown by Hollow & Graham. *Packer et al* (1964) also used a 7 5 g weight These authors draw attention to the tendency which is often met with in Schiotz tonometry towards a preference for whole rather than half scale unit readings which manifests itself in an uneven distribution curve with several maxima and minima Such a tendency is clearly apparent in the large Finnish survey (Katavisto et al) In the present work it will be seen that the tendency has been eliminated to a reasonable extent since the most pronounced minima in the curves of fig 4 correspond to scale units 8½ 8 and 8 and the course of the curve in fig 5 is quite smooth

It would hardly have been possible to obtain the present results from Umanaq by means of an applanation tonometer of the Goldmann type The working conditions *are* primitive In a few cases persons had to be sought out in their homes and the measurements made on the sleeping platform¹

The *tension indicator* was used from a desire to be able also by measuring on the applanation principle to delimit a group of persons with increased pres

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sures The results obtained will be dealt with in a subsequent article, but a simple evaluation from the point of view of measuring technique will be given

As regards the 79 eyes in which the applanation pressure was found by the tension indicator to be 21 mm Hg it is interesting to see the *Schiotz values* Fig 6 shows such a comparison The mean value is near 21 mm but the dis *persion is considerable*

One of the reasons for this may be found in the low accuracy of the reading because of the low magnification (× 3) and low light intensity of the instru ment *(Bruun Jensen 1968) It should be noticed however that Schwart. & Dell Osso* (1966) found an only slightly smaller dispersion of the difference between paired applanation and Schiotz measurements made on supine persons (2 54 mm Hg) They mention that the dispersion *may in particular be caused* by the fairly considerable dependence of Schiotz tonometry on the rigidity of the eye Incidentally the authors found the applanation pressure in supine po sition to be on an average 3 mm higher than the Schiotz value (and in sitting position 1 1 mm higher than the Schiotz value confer Hollows & Graham in table 3) *On this basis the dispersion found in the present* small material can not be said to be surprising It *is* strange however that the mean value of the Schiotz values found is actually approximately equal to the adjustment value 21 mm of the tension indicator

On the whole the author of the present study found the tension indicator to

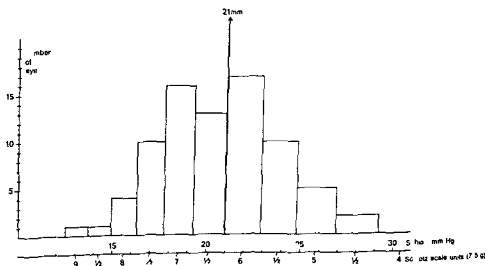


Fig 6

Tension indicator versus Schiotz tonometer Distribution of Schiotz intraocular pressure for 79 eyes with *applanation pressure = 21 mm Hg* ($\bar{x}$ = *20 4 mm Hg s e* = 0 35 mm Hg s = 3 15 mm Hg)

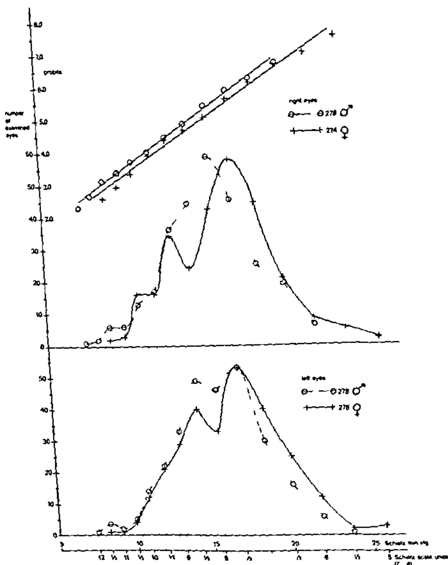


Fig 4

Int aocular pressure of normal eyes Separate curves for right and left eyes of men and women without diagnosis of glaucoma and without major corneal alterations i e tonomet ically normal eyes As regard right eyes distribution curves in probits show good approximation to straight lines

be suitable for the purpose and more convenient to use than the Schiotz tonometer With improved optics and illumination it would be a very valuable instrument particularly under primitive conditions as in Greenland

Conclusion

In a survey of the population of a medical district in Greenland with more than 95 per cent participation it has been shown that measured with a Schiotz tonometer the mean tension of normal eyes in Greenlanders *is 15 7 mm Hg* with a standard deviation of 3 0 mm The results correspond exactly to those found in surveys of other populations An *analysis of the sub groups* of the sample concerned has further shown that the eyes of women above forty years of age show a *significantly higher tension* than those of men (mean values ♀ 16 35 mm and ♂ 15 1 mm) just as the dispersion in the case of this female group is slightly greater than that of the male group (s♀ - 3 3 mm Hg and s♂ = ?8 mm Hg)

Summary

Motivated by our knowledge of the great part which glaucoma plays in the problem of blindness in Greenland – and directly occasioned by a number of severe glaucoma attacks – the author carried out a glaucoma screening in the district of Umanaq in 1967 More than 95 per cent of the population above twenty *years of age in the town* and *above forty years* of age in the villages took part.

The geography population and health service of the district as well as the method and material of the survey are mentioned briefly

On the basis of 1108 normal eyes the mean value of the normal tension is calculated in the two sexes and in different age groups It is concluded that this population of mixed Eskimoic Caucasian origin as regards the parameters mentioned gives the same results as other population groups which have been studied As elsewhere the ocular tension has been found to be significantly higher in women than in men in the age group above forty

Finally the limitations incident to the Schiotz tonometry used for the present study are discussed in relation to applanation *tonometry and the results obtained* by means of Bruun Jensen s tension indicator according to this principle are mentioned

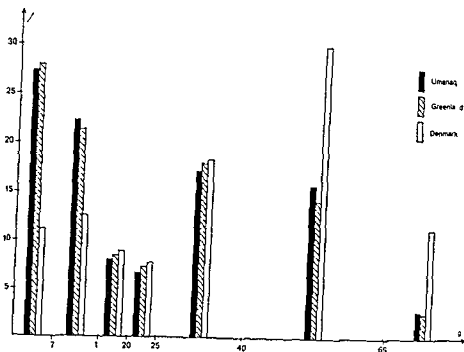


Fig 2

Percentage distribution of age from census 31 Dec 1965 (Number of inhabitants Umanaq 2150 Greenland 35 117 Denmark 4 7/9 399)

Fig 3

Umanaq hospital with 33 beds in front of the mountain (11/5 metres) which dominates the island (Photo Ib Faurholt)

Acknowledgments

Department Nurse Eva Steenstrup Umanaq has given me invaluable assistance both as regards the actual examinations and in the arrangement of the material

I thank Mr Villy Hansen cand polit the Ministry for Greenland for assistance with the statistical work

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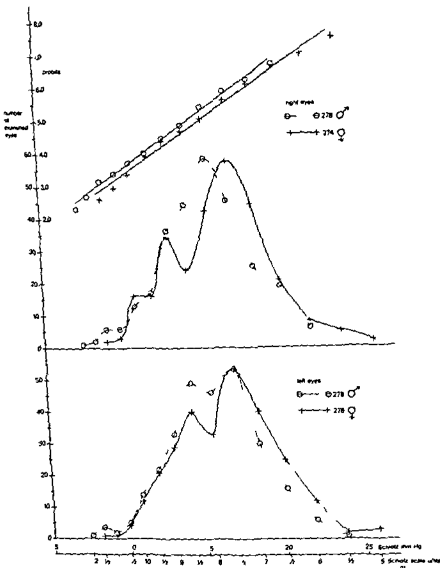


Fig 4

Intraocular pressure of normal eyes Separate curves for right and left eyes of men and women without diagnosis of glaucoma and without major corneal alterations i e tonometrically normal eyes As regard right eyes distribution curves in probits show good approximation to straight lines

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On account of small errors detected later on the actual deficit is slightly greater than the above mentioned six but the number of persons examined corresponds certainly to more than 95 per cent of the population of the district within the age groups concerned

5) Results

The necessary more detailed ophthalmological examinations and the evaluation of the results were made by V Clemmesen during a fortnight in August September 1967 As a final result the prevalence of angle closure glaucoma and open angle glaucoma was found to be 10 per cent (19/192) and 1 5 per cent (3/192) respectively among women and 0 per cent and 1 per cent (2/204) among men in the age group above forty Out of the altogether 26 primary glaucoma cases 15 were not known before the screening Principles of glaucoma classification and case records will be given in subsequent publications (Alsbirk Clemmesen)

Intraocular Pressure in Normal Eyes in Greenlanders Determined by Schiotz Tonometry

When all persons suffering from primary glaucoma (26) and all eyes (= 8) with severe alterations of the cornea and possible secondary glaucoma had been excluded the remaining number of eyes were 1108 The intraocular pressure was calculated on the basis of this sample Fig 4 and table II illustrate the results The curves agree sufficiently closely with the Gaussian distribution to justify the use of the corresponding calculations Since the intraocular pressures of the right and left eyes of a person cannot be considered as independent variables the calculations have been made separately for right and left eyes (conf *Hollows & Graham* 1966) As it will be seen no difference was observed between right and left while there is a significant difference between the mean values for women and for men the mean tension in female eyes being 16 1 ± 0 19 mm Hg as against 15 2 and 15 3 ± 0 17 mm Hg in male eyes As will appear this difference between the sexes is evident in the age groups above forty but does not appear in the youngest group

Measured by the standard deviation the biological dispersion in the group above forty is greater for women than for men and this difference is significant (most clearly with regard to left eyes $P < 0\ 01$)

Tension above $\bar{x} + 2s$ and $\bar{x} + 3s$ may be anticipated statistically in 2 28 and 0 14 per cent of normal eyes These limiting values correspond in the case of men to 21 1 and 24 0 mm Hg and in the case of women to 22 4 and 25 6 mm Hg

It was theoretically possible that the town population which was examined

From the I Eye Clinic Medical University School Budapest Hungary
(Director Prof Dr M Radnot)

POLARIZING MICROSCOPIC STUDIES ON THE REGENERATION BEHAVIOUR OF PERFORATING CORNEAL WOUNDS

BY

MARGARET VARGA and J FEHÉR

The polarizing microscopic techniques came into prominence in the field of the morphological research in recent years This fact can mainly be attributed to technical reasons

The use of the so called "topooptical reactions" based on oriented colour binding considerably extended the possibilities of this technique and presented further informations to electron microscopic findings one of the most important methods for submicroscopic structural research

The development of the topooptical reactions was the result of *Romhanyi's* work (1966) We can give its essentials as follows

Treating the preparations with suitable colouring agents of molecular configurations (toluidin blue rivanol azur methylen blue thiosin etc) the molecules of the colouring agents will link to each of the constituents of the preparation in a patterned array The oriented binding of the colours results in a change of the anisotropy of the structure The initial birefringence will increase or decrease possibly reverse The topooptical reactions indicate very poor or even latent birefringences selectively Topooptical reactions by polarizing optical techniques make possible the study of a number of structural peculiarities which hitherto were unacessible Thus the structure of the interfibrillar substance of the connective tissue and the peculiarities of the lipoprotein membranes *etc* could be better understood

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Table II

Intraocular pressure of normal eyes by Schiotz tonometer

Age group		Women right	Women left	Men right	Men left	Comparison between women and men Significance test
0–39	x	15.8	15.5	15.7	15.5	$P_l < 0.2$
	s	2.9	2.8	3.0	3.3	
	n	107	107	80	80	
40–49	x	16.2	16.3	14.7	14.8	$P = P_l < 0.005$
50–59	x	*16.4*	16.8	15.4	15.6	$P_l < 0.05 < P_r < 0.1$
60+	x	16.2	16.2	15.0	15.2	$P < 0.05 < P_l < 0.1$
40+	x	16.3	16.4	15.0	15.2	$P_r = P_l < 0.0005$
	s.e.	0.25	0.26	0.20	0.19	
	s	3.3	3.4	2.8	2.7	$P_l < 0.01 < P_r < 0.05$
	n	167	169	198	200	
20+	x	16.1	16.1	15.2	15.3	$P < 0.001 < P_l < 0.005$
	s.e.	0.19	0.19	0.17	0.17	
	s	3.1	3.2	2.9	2.9	$P_r = P_l < 0.2$
	n	274	276	278	280	

x = mean value (mm Hg)
s.e. = standard error of mean (mm Hg)
s = standard deviation (mm Hg)
n = number of eyes examined
P = probability (for right eyes two tailed test)
P_l = probability (for left eyes two tailed test)
(P values according to Student distribution for degrees of freedom ≤ 200
P values according to normal distribution for degrees of freedom > 200
Tables Documenta Geigy 6 ed Basel 1962)

during the dark period might have displayed intraocular pressures which differed from those of the inhabitants of the villages who were as mentioned examined in the summer It might be imagined for instance that an effect similar to that of a dark room test on many narrow angles would result in a higher intraocular pressure in the group observed during the dark period or that other seasonal factors might influence the tension However the present results do not support any theories of that kind the mean tensions differing

These examples suggest the method renders it possible to study areas which are difficult to access by other techniques

The polarizing optical methods were used in studying the collagen fibres of the stroma and keratocytes.

1 The study of the collagen fibres

a) Protein fibrils

The phenol reaction is very useful to study the protein fibrils of the col lagen This is one of the earliest polarizing optical techniques (*Ebner* 1894) The phenol molecules being built in between the adjacent keto imido groups of the protein chains of the collagen fibrils reverse the initially positive birefringence to negative simultaneously increasing it The phenol reaction is specific to the collagen

b) Interfibrillar substance

Consists of biochemically acid mucopolysaccharides called often by different authors as ground substance Kittsubstanz" and is believed to be amorph *Romhanyi* (1963) verified the structural characteristics of the interfibrillar substance with polarizing optical techniques His results indicate that acid mucopolysaccharide chains are parallelly arranged to the fibrils of the intra and interfibrillar substance Various basic colour agents mostly toluidin blue and rivanol enlighten the study of the interfibrillar substance (by polarizing optical techniques) by binding isolatedly to it

Information is furnished on the fibril forming process by the phenol reaction and on the forming of the interfibrillar substance by the toluidin blue and riva nol staining (anisotropic staining) respectively

2. The study of the keratocytes

a) Examination of the structural lipoids

Romhanyi & Deak (1967) developed the topooptical reactions which give the opportunity of studying the lipo protein membranes by polarizing optical tech niques They used various basic colour agents with an after treatment by potas sium ferricyanide or by a mixture of potassium iodide potassium ferricyanide The after treatment fixes the colour linkages on the structure In the topooptical reactions of the lipoprotein membranes the protein part of the membrane and the lipoids as well are responsible for the binding and the orientation of the colouring agent respectively The method is useful for studying basal mem branes cell membranes ergastoplasm mitochondria and other cytomembranes

b) Examination of the activity of the keratocytes

The anisotropy of the keratocytes became evident during the studies of the cornea for other purposes This casual observation gave us the impulse to study

hours After 3 4 days the patients were sent home The first pigmentations are then in most cases already clearly visible in the borders of the coagulated areas After a fortnight the patients were allowed to return to work

In two cases the method has been used to complete the delimitations of de tachments operated upon after Custodis with cryo treatment under the silicon plomb In one case with aphacia a small flat detachment with two peripheric tears was circumscribed All cases of retinal ruptures with and without detach ment have healed completely without complications and with unchanged or im proved vision

Recently we have begun to treat diabetic retinopathy both cases with proli ferative vessels on the disc and cases with other alterations of the fundus In these cases retrobulbar anaesthesia with Xylocain®* 2% with epinephrine has been given The results seem promising but the observation time has been short

In all cases treated with the Fankhauser Lotmar device no complication whatsoever has occurred The apparatus has worked with great safety and re liability and has never failed The method has proved much easier than the usual photocoagulation with the Zeiss apparatus in the hand of a trained bio *microscopist* All cases of retinal detachments and ruptures have healed and no recurrences have occurred The apparatus will soon be made for sale** It has proved to be an excellent device for rapid and exact photocoagulation first and foremost in cases with extremely peripheric lesions in which Eisner s funnel can be of good help but also in lesions of the central fundus

Summary

Photocoagulation with the device of Fankhauser and Lotmar is described The great advantages of this method over the usual photocoagulation especially in cases with peripheric lesions are emphasized

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Fankh [illegible] *F & Lotmar* [illegible] th to oagulati n Thr ugh the G ldmann Contact Glass AMA A h Ophthal [illegible] 350 196[illegible]

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* L [illegible] n (Astra Sweden)

** M nufa tu e l by SADAMEL, Rue Jardiniere 130 La Chaux de Fon ls Switzerlan l

tact glass is made very easily. By using Eisner's indentor funnel (Fig. 3) which is to be slipped over the contact glass, photocoagulation is possible without any difficulty even on the pars plana in cases with clear lenses. This funnel offers two advantages: (1) the eyeball is immobilized by suction and (2) the sclera may be indented at variable distances from the ciliary body. A red spot in the slit image on the retina indicates the area to be coagulated. An inbuilt cobalt blue filter makes coagulation possible during fluorescein angiography. Even in cases with cataract, clear zones between the cataractous spokes may be used for photocoagulation by slightly tilting the contact glass.

In 11 eyes 14 peripheric retinal ruptures without detachment but with marked vitreous tractions have been treated. All these ruptures were complications to an acute posterior vitreous detachment. In one eye multiple breaks after a contusion were coagulated. In many cases the tears were so peripheric that coagulations had to be made on the pars plana with the aid of Eisner's funnel to circumscribe the lesions. The ruptures were easily found in all cases and treated without difficulty. In most cases the field stop on the Zeiss photocoagulator was put on 1.5° corresponding to 3.6° (1.06 mm) when the Fankhauser Lotmar device is used, or more seldom on 0.5° corresponding to 1.2° (0.35 mm). The intensity "red II" of the photocoagulator was used in most cases. Only in a few dark fundi was "red I" chosen. The iris stop of the coagulator was used fully open. The high intensity makes the use of very short times possible, which is of importance since the eye treated is immobilized only by the contact glass. In all cases with peripheric retinal ruptures local anaesthesia with Novesin®* 0.4% was used. After the treatment the patients were kept in bed for about 24

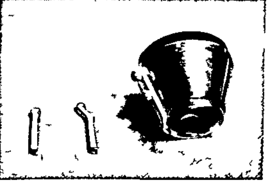


Fig. 3
Eisner's funnel slightly modified. The indentors of different lengths are interchangeable.

* Oxibuprocaine (Wander, Switzerland)

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keratocytes between the swelled fibres compared with the intact areas seemed unchanged or slightly decreased

After 1⁹ hours In relation to the previous tate no deviation was evident by *polarizing optical technique*

After 24 hours (Fig 1) The corneal stroma swelled the anisotropy of the fibres unchanged The anisotropy of the keratocytes adjacent to the edges of the wound increased The shape and size of the keratocytes practically agreed with those of the intact area except for the increased birefringence

After 48 hours (Fig 2) The swelling of the stroma has not changed The area between the edges of the wound reveals insotropy with very poor birefringence of the clumped fibrin here and there

The increased anisotropy of the keratocytes could be observed in the stroma close to the wound The keratocytes were slightly widened and lengthened These phenomena could be found in the neighbourhood of the wound only keratocytes did not display any changes at all beyond that toward the limbus

After 7 days (Fig 3) The neighbourhood of the wound was swelled the fibres were loosened The upper quarter of the area between the edges of the wound was filled with penetrating epithelium processes Under this area the



Fig 1

The increased anisotropy of the keratocytes becomes evident among dark compensated *fibres* C R I comp Polar micrograph Toluidin blue colouring Abt 800 ×

Eye Clinic Medical Faculty Rotterdam

VARIABILITY OF THE ELECTRO OCULOGRAM (EOG)

BY

G H M VAN LITH and J BALIK

Introduction

Electro oculography developed by Arden in 1962 is a useful and worthwhile method in clinical practice

By measuring not the standing potential itself but the increase during light adaptation as expressed in the light peak dark trough ratio (LP/DT ratio) individual variations are diminished Nevertheless variations between individuals and in the same individual are rather high (*Elenius* 1962 *Kelsey* 1967) As the variations in the EOG when determined in one and the same person are important in view of the check on chloroquine intoxication a confirmation of Kelsey s data seems valuable A preliminary report was already published (*Henkes et al* 1968)

Method

Examination was done in 15 normal subjects (9 ♂ and 6♀) varying in age from 21 to 48 From each of them 10 EOG s were obtained according to Arden s technique on different days and different daytimes in the course of some weeks The light peak dark trough ratio which normally is about 2 00 with a lower limit of the normal range of 1 85 was calculated (*Arden* 1962)

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the problem (*Feher & Varga* 1969) It was found that the lipoprotein lamellas of the cell organella (ergastoplasm mitochondrium etc) are responsible for the anisotropy of the keratocytes The possibility to examine the organella by polarizing optical means is due to the fact that the organella are arranged lengthwise even in the longitudinally extending cells as well shown by electron photomicrography The quantity of the cell organella may be concluded from the extent and degree of the anisotropy In turn the quantity of the organella is indicative for the metabolism or activity of the cell

On the basis of the above considerations the activity and fibroblastic function of the cell might be deduced from the anisotropy of the keratocytes

Material and Methods

Perforating lesions were made on the central area of the corneas of 28 rabbits, 3 mm of length in each case

The eyes were enucleated after 2 12 24 48 hours and 1 2 4 weeks respectively The removal of the eyes was then followed by processing with polarizing optical techniques

The globes were fixed in neutral formol of 1 4 Refrigerated sections were cut of 10 μ thickness partly after having been embedded in gelatine and partly without gelatine

The native examinations were executed after covering with acaci gum and glycerol

Topooptical reactions phenol reaction according to *Ebner* (1894) rivanol colouring according to *Romhanyi 1962* (Rivanol *0 1 Mol* precipitated *with potassium* ferricyanide of 2 %) colouring with toluidin blue according to *Romhanyi* 1962 (toluidin blue colour solved in Michaelis veronal potassium acetate buffer of 3 5–6 pH to 0 01 % concentration precipitated with potassium ferricyanide *of 2 %* or with a mixture of 1 7 from potassium ferricyanide and potassium iodide)

The extraction of the lipoid was accomplished in a mixture of 3 1 chloroform metanol during 24 hours in room temperature

Observations

After 2 hours The corneal stroma adjacent to the wound swelled approximately to the double Changes of anisotropy were not perceptible The anisotropy of the

Results

The variability per individual was rather high Figure 1 gives an impression of this variability For each subject the mean value and the standard deviation were determined for the right and left eye separately (figure 2) The mean value of subject 15 proved to be significantly higher than those of the other subjects This difference is statistically verified For this reason the results of this subject were omitted in further calculations The mean value and standard deviation of all 140 experiments were respectively 2 15 and 0 25 These results are of the same order as Kelsey's

With these experiments as a basis two conclusions can be drawn When only one EOG is determined values below 1 85 cannot be said to be abnormal To be sure if the result is pathological two times the standard deviation has to be subtracted from the mean value and to be quite sure even three times the standard deviation This means that a value lower than 1 65 is highly probably abnormal an a value lower than 1 40 surely is Values between 1 65 and 1 90 are borderline cases The second conclusion is that an alteration of the EOG lower than 0 25 in the same person has no particular meaning An alteration of more than 0 25 is remarkable of more than 0 50 is of much value

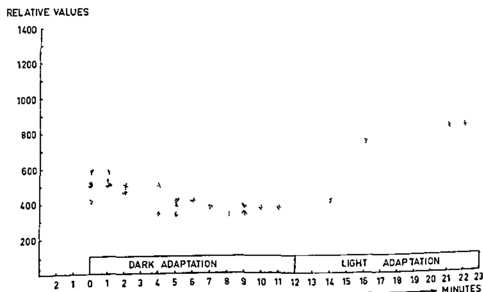


Fig 1

Standing potentials measured and plotted in relative values during 12 minutes dark adaptation and 12 minutes light adaptation Before dark adaptation the subjects are light adapted during 10 minutes

fibroblast mass was surrounded by a substance of mucoid character Some very fine fibrils were seen crossing the mucoid substance Near the edges of the wound there was a number of *active keratocytes among the parted stroma* fibres

After 14 days The area between the edges of the wound was filled with cicatrized tissue crossed only by thin collagen bridges (fig 4) which were arranged corresponding to the original fibre pattern Between the collagen fibrils *however abundant mucoid substance was shown following the regular fibre* arrangement (fig 5) Numerous fibroblast were seen in the freshly grown connective tissue (fig 6) The fibres of the stroma adjacent to the wound were still swollen among them a number of elongated thickened keratocytes of strong anisotropy

After 28 days The collagen fibrils were increased and strengthened in the cicatrized tissue between the edges of the wound (fig 7) The interfibrillar substance too was oriented along the fibres As before there were many fibroblasts in the cicatrized tissue The stroma swelled in the vicinity of the wound Among the fibres there were many keratocytes in the area corresponding to the swollen stroma with widened and elongated plasma *showing strong aniso*tropy (fig 8)



Fig 4
Thin collagen fibrils between the edges of the wound Polar micrograph
Phenol reaction Abt 600 ×

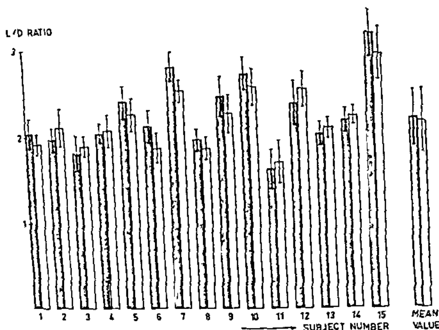


Fig 2

Mean values and standard deviation (vertical bar) of the light peak/dark trough ratio of 10 experiments in each of 15 subjects (shaded block right eye white block left eye)

Causes of variability

In order to diminish these great variations their possible causes were examined

The position of the electrode surely alters the height of the standing potential If only the LP/DT ratio is measured no essential influence can be expected To check this point 5 EOG s were determined in 9 subjects directly after each other with the electrodes remaining at the same place in one afternoon Only the results of those 5 subjects from whom also 10 EOG s were determined on different days are given in the table The standard deviations of the 5 EOG s made in one afternoon appeared to be not smaller than those of the 10 EOG s The conclusion must be that replacing the electrodes is not very influencial

A peculiar phenomenon was that the 2nd and 5th EOG were always higher than the others The difference between the 1st 3rd and 4th EOG was not statistically significant A clear explanation for the high values obtained in the 2nd and 5th EOG cannot be given

A second variable factor may be the adaptive state before the darkadaptation time starts From literature (*Kris* 1960) it is known that – like the increase



Fig 2

Elongated keratocytes among the corneal fibres The fibres are dark the keratocytes are compensated to brightness G R I comp Polar micrograph Toluidin blue colouring *Abt 800* ×

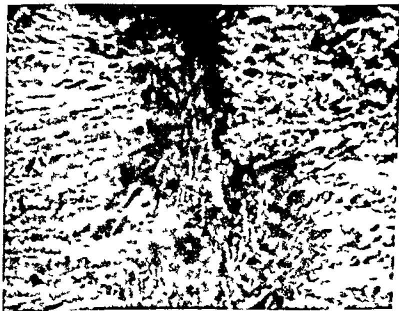


Fig 3

Fibroblast mass between the edges of the wound Much active keratocytes are between the aparted fibres Polar micrograph Toluidin blue colouring Abt 400 ×

Table I

subject number	mean of 10 ×	stand dev	mean of 5 ×	stand dev
10	2 62	0 20	2 67	0 19
11	1 64	0 23	1 84	0 14
12	2 42	0 24	2 95	0 16
13	2 04	0 13	2 37	0 12
14	2 17	0 13	2 64	0 26

during lightadaptation – also an increase can be observed going from the light adapted state to the darkadapted state Such an increase may interfere with the light peak dark trough ratio which has to be measured Therefore in 5 subjects the standing potential has been measured in 13 experiments while in stead of *light adaptation after 12 minutes the lights stay off Before dark adaptation the* subjects were light adapted during 10 minutes

Figure 3 is an example from one subject For the 5 subjects the mean increase was between 0 348 and 0 387 and was significant at a 1 per cent level Because this increase occurs at the same time as normally the light peak can be

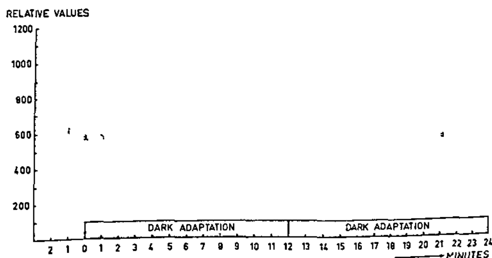


Fig 3
Standing potentials in relative values during 24 minutes dark adaptation Before dark adaptation the subjects are light adapted during 10 minutes

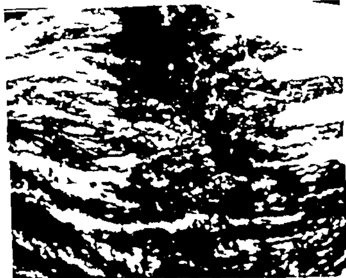


Fig 7

Thickened and multiplied collagen fibrils between the edges of the wound Polar micrograph Phenol reaction Abt 600 ×



Fig 8

Enormous number of fibroblasts in the scar tissue and the surroundings Polar micrograph Toluidin blue colouring Abt 600 ×

expected it will be clear that the *adaptive state before* dark adaptation starts is an important factor

To see whether the time of day was of influence all experiments were grouped according to day hours (fig 4) Correlation was determined by mean *of Spearman s coefficient of correlation* (R = 0 709) *This means* that *variability* during the day is proved for 50 per cent Hence if possible one should try and examine and re examine the patients during the same time of the day

Other factors which may be involved with the great variations occurring in *EOG examinations are difficult to measure or to prevent* For instance the change in the electrical resistance of the skin dependent on the degree of per spiration the possible occurrence of a flood of tears making contact with the nasal electrode and the ability to keep the eyes open during the early minutes of light adaptation The last *mentioned factor may influence* the *rapidity* of retinal bleaching and so the height of the light peak in the EOG

A last factor causing variations in the EOG finally is the patient s self con *trol in moving only his eyes and not his head*

Summary

Variability of the EOG has been determined by making 10 EOG s in each of 15 normal subjects The mean value and standard deviation of the experiments was respectively 2 15 and 0 25 From the results two conclusions have been

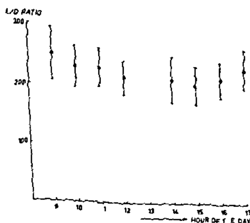


Fig 4

Light peak dark trough ratio according to day hours Vertical bars standard deviation



Fig 5

The interfibrillar substance in the cicatrized tissue shows distinct anisotropy Polar micrograph Toluidin blue colouring Abt 600 ×



Fig 6

The fibroblasts in the scar tissue and the surroundings exhibit strong anisotropy G R I comp Polar micrograph Toluidin blue colouring Abt 600 ×

drawn Firstly values lower than 1 65 are highly probably abnormal lower than 1 40 surely are Secondly only an alteration of the EOG of more than 0 25 in the same person has particular meaning

Some factors which may cause these rather great variations have been examined

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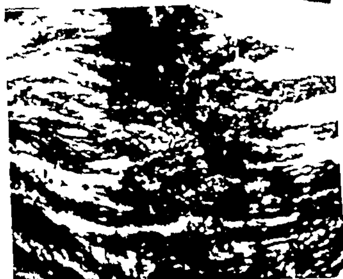


Fig 7
Thickened and multiplied collagen fibrils between the edges of the wound Polar micrograph Phenol reaction Abt 600 ×



Fig 8
Enormous number of fibroblasts in the scar tissue and the surroundings Polar micrograph Toluidin blue colouring Abt 600 ×

Eye Clinic Medical Faculty Rotterdam

THE INFLUENCE OF GLUCOSE LOADING ON THE ELECTRO OCULOGRAPHIC RATIO (EOG) IN NORMAL SUBJECTS AND DIABETICS

BY

J BALIK and G H M VAN LITH

Introduction

The determination of the light peak dark trough ratio (LP/DT ratio) in the EOG can be a suitable supplement of a general functional examination in diabetes mellitus The standing potential is usually low mostly it shows a greater decrease in long term diabetes with serious diabetic retinopathy

The LP/DT ratio too is found to be lowered the light peak time often delayed (6) A correlation between the LP/DT ratio and the blood sugar level after an oral glucose tolerance test could not be proved (4) However after an intravenous glucose infusion reaching much higher blood sugar levels it appeared that in normal individuals the LP/DT ratio increased significantly while in diabetics it did not (5)

Only a small number of eyes was examined at that time Limiting the investigation only to the EOG we have now examined and compared a larger group of diabetics and normal subjects

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Discussion

Following perforating corneal injuries the healing of the stroma takes its course with cicatrization The fibroblasts are responsible for the forming of the cicatrized tissue The origin of the fibroblasts has been the subject of much discussion

According to the observation of *Weimar* (1957, 1958 1959 1960 1962 1965 1966) 24 hours after the lesion about 75 per cent of the keratocytes transform into fibroblasts in the surroundings of the wound By histochemical examinations *Kitano* (1966) *Kitano* & *Goldman* (1966) proved that all the fibroblasts which contributed to the healing of the wound originated from the transformation of the keratocytes

In addition, it was assumed that the transformation of other cells (first of all macrophags) is responsible for the formation of fibroblasts (*Pullinger* & *Mann* 1943 *Duke-Elder* 1954 *Weimar* 1958) The macrophags originated partly from the monocytes of the blood partly they were histiocytes of RES origin (*Nemeth* 1936 *Boros* & *Takats* 1951) *Salzer* (1937) assumed that the fibroblasts may develop from the transforming epithelial cells

Autoradiographic investigations of *Robb* & *Kuwabara* (1964) have shown that the epithelial cells of the cornea never transformed into fibroblasts and when the corneal wound is situated in the central area the mononuclear cells do not contribute to the healing In the case of peripheral wounds the authors do not preclude this possibility

The first sign of the beginning of the production of cicatrized tissue is the increasing activity of the keratocytes The activating factor(s) are produced by the injured epithelium (*Weimar* *Davis* & *Haraguchi* 1965) In the activated keratocytes there begins a strong metabolic function with newly developed enzymesystems

During our studies changes could be observed by polarizing optical techniques as soon as 24 hours after the lesion The anisotropy of the keratocytes near to the wound increased without a change of the shape or size of the cell The anisotropy of the keratocytes is due to the cell organella hence the increasing anisotropy indicates the growing of the former and the more intense metabolic activity as well The keratocytes after 48 hours become longer and broader with forms exhibiting mitotic activity

Dunnington & *Smelser* (1958) proved that the synthesis of the mucopolysaccharides begins with the activation of the keratocytes By using autoradiography they observed the take up of S^{35} labelled sulphate in the narrow zone surrounding the wound 24 or rather 48 hours after the lesion which fact was an evidence for the synthesis of sulphated mucopolysaccharides The fibre synthesis equally begins with the production of the ground substance

On the second day the fibroblasts are beginning to synthetize the collagen

Methods

FOG was examined by means of Arden s technique (1 2) in 16 normal persons (27 eyes – 15 men aged 22 to 50 and 1 woman of 28) and in 20 diabetics (39 eyes - 9 men and 11 women varying in age from 33 to 63)

Firstly the EOG was determined without glucose loading After this initial examination 500 ml 30 per cent glucose solution was given in 45 minutes during which time the second FOG was determined The blood sugar level was examined before the first LOG, after the DA time of the second EOG (approximately halftime of the glucose infusion) and at the end of the second FOG (approximately at the end of the glucose infusion) by means of the glucose oxidase method The mean value of the latter two findings was taken into consideration As the value after glucose loading also depends on the value before glucose loading only the difference in both values was taken into account and verified by means of Student s t test

Qualitative changes (increase or decrease of the EOG) in both groups were verified by means of the χ^2 test The correlation between the EOG and the difference of the blood sugar levels in the loading tests was determined by Spearman s correlation test The results of the examination of both groups are given in the table the statistical results in the text

Results

The difference of the mean value of the LP/DT ratio between the control and the diabetic group before loading was 49 7 This difference is statistically significant ($t = 4\ 920 > 2\ 043$ for 66 degrees of freedom) Also the variance

Table 1

LP/DT ratio	decreased	increased	
diabetics	4	23	27
control	23	16	39
	27	39	66

precursor At first this soluble substance of protein character is secreted into the extracellular spaces and then aggregates into a fibrous structure

According to our examinations on the sixth day following the lesion the area between the edges of the wound is filled up with a cell mass consisting of fibroblasts Among the fibres of the swollen collagen adjacent to the wound there are a number of fibroblastic transformed keratocytes The fibroblasts are surrounded by mucoid substance in which sparse fibrils can be detected by pora rizing technique

In the later stages of the regeneration the growing of the fibroblasts and the increase of the cicatrized tissue become evident At first in the newly formed cicatrized tissue there are few fibrils but then they increase in number more and more The fibrils are thickened gradually and follow the pattern of the intact fibres The arrangement of the fibres in the scar is possibly due to the force exerced by the intraocular pressure to the cornea (*Payrau et al* 1967) The ranging of the fibres is accompanied by the gradual clearing off of the scar

Summary

The authors investigated the perforating corneal wound in the central area by polarizing optical techniques The results show that the phenomena of regenera tion originate from the keratocytes of the stroma near the wound The activity of the keratocytes increases the cells multiply and their fibroblastic activity produces the scar tissue The collagen fibres gradually grow and strengthen in the mucoid of the cicatrized tissue

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difference of both groups (F = 2 67 for 28 and 38 degrees of freedom) shows a difference between the normal subjects and the diabetics

Examining the control group in the fasting state (27 eyes) the mean value of the LP/DT ratio was 211 9 (standard deviation 47 6) *after glucose loading* the ratio was increased by 23 6 (standard deviation 41 6) this increase is statistically significant (t= 3 06 for 28 degrees of freedom) The correlation factor R between the increase in the LP/DT ratio and the blood sugar level was 0 50 (δ 1 96 = 0 46452 < 0 50)

The mean value of the LP/DT ratio in *the diabetic group before glucose* loading (39 eyes) was 162 2 (standard deviation 29 1) after glucose loading the mean increase was 2 7 (standard deviation 30 9) This increase does not differ from zero (t = 0 545 for 38 degrees of freedom) The correlation factor R between the amount in which the LP/DT ratio and the blood sugar level increase after loading was 0 115 (0 539 – statistically not significant) χ = *1° 870 for 1 degree of freedom By means of this test it is statistically proved* that the LP/DT ratio increases during glucose loading more often in the control group than in diabetics

Discussion

From these results we can conclude that the LP/DT ratio in the EOG is lower in diabetics than in a control group While in the control groups this ratio is *increased significantly* and quite often by *means of intravenous glucose* infusion it does not increase in diabetics it even decreases sometimes The increase in the LP/DT ratio of the control group has not a significant correlation with the increase in the blood sugar level during the loading

It is rather difficult to explain exactly the changes found because little knowledge exists about the nature of processes which determine the height of the standing potential and its alteration during light adaptation If we consider that the EOG originates in the border layer between retina and choriocapillaris (in the pigment epithelium) and that it can be changed by influences on both sides (7) we can possibly explain the results obtained by means of theoretical knowledge of the difference in metabolic processes which exist between the normal and diabetic retina Both retinas are insensitive to blood sugar changes and to the presence of insulin (3) This explains *why only* a small perhaps no correlation exists between the LP/DT ratio and the blood sugar level

However changes in secondary metabolic glucose processes (energy shifting during phosphorylation and changes in the relation between oxidized and

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DENDRITIC (HERPETIC) KERATITIS

I Incidence – Seasonal Variations – Recurrence Rate – Visual Impairment – Therapy

BY

M S NORN

Herpetic keratitis is a frequent disease often causing lost working days The disease represents a steadily increasing problem within our highly advanced social system where other diseases are combated with greater success

The present possibility of instituting rational treatment with 5 iodo 2 deoxyuridine (IDU) which interferes direct with the viral metabolism is regarded as a great improvement

Numerous reports have been published on this subject since *Kaufman et al* (19‹?) introduced IDU treatment against dendritic keratitis A favourable result has been noticed in most cases (*Kaufman Insetli et al Cappercucci Mach et al Laibson et al Maxwell Patterson et al Sood et al* etc)

The response to IDU has been studied through double blind trials using as placebo water or substances of at least doubtful therapeutic value

These trials have shown IDU to give more rapid cure than placebo (*Patterson Laibson Jepson Hart et al Davidson Burns*)

Fy et al and *Macken ie* took up a more reserved attitude The latter found cauterisation to have a better effect than IDU *Cilkes* found no significant difference between the effects of iodine cauterisation and IDU therapy

Some workers state that a favourable response to IDU is only obtainable

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reduzed coenzym nicotinamid adenin dinucleoted in oxidizing of fat acids) can influence the normal semipermeable membrane causing an increase in potential difference on either side of the membrane This may explain the increase in the standing potential of the normal retina during light adaptation and in the LP/DT ratio after glucose loading

In diabetes permeability of the capillary membrane is increased this results in a free and uncontrolled transport of water and ions Also the ability to maintain differences in concentration supported by means of released energy during the glucose metabolism and redox potential changes is diminished Because in this situation the secondary metabolic processes after glucose loading could not make themselves valid the standing potential remains low and does not show the same increase as in the normal subjects It is namely known that the relation between NAD NADH_ and NADPH NDAP is diminished in diabetes due to a relative increase in NADH and a relative decrease in NADPH. (3) The permeability of the capillary membrane is increased due to the storage of collagen glycoprotein with a large content of hydroxyproline

The decrease in the LP/DT ratio during glucose loading in the control group is only occasional in diabetics however significant This decrease is probably a specific symptom for the diabetic retinopathy It may be that in diabetics secondary metabolic processes even get worse during the loading

Considering the known changes of semipermeable membranes and the results mentioned here it may be possible to determine the quality of the permeability of these membranes by means of the EOG Perhaps it may be possible to check their function during the course of the disease

We surely do not assert that a lowered LP/DT ratio is always the result of the above mentioned processes Other causes for a lowered ratio may be a lowered activity of the receptors a lowered circulation in the choriocapillaris and a lowered electrical resistance between the retina and the choriocapillaris resulting in an inability to retain a potential difference

Summary

The light peak dark trough ratio of the EOG has been examined in a group of normal subjects and in a group of diabetic patients before and after intravenous glucose loading In the normal group this ratio appeared to be significantly higher after the loading than before In the diabetic group no significant increase could be observed In the discussion an attempt is made to explain this difference between the normal subject and the diabetic patient

Table III

Effect of antiglaucomatous treatment on the thickness of the corneal stroma in normal eyes

			Before treatment		After treatment		ΔT (μ)
			IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
EO	m	os	14	466	12	470	4
HB	f	os	17	466	12	464	− 2
FK	m	os	12	472	10	478	6
IS	m	os	15	434	13	432	− 2
LB	m	od	13	470	10	480	10
MB	f	os	16	450	12	446	− 4
GK	f	os	18	430	14	426	− 4
IK	m	os	18	490	14	490	0
IS	f	od	16	408	13	408	0
mean			15	454 ± 9	12	454 ± 9	1 ± 2

The table shows corresponding values of IOP and thickness of corneal stroma in normal eyes before and after treatment for 2 days with pilocarpine acetazolamide and adrenaline Lower line mean ± standard error of mean

Results

Table I shows data for 8 patients in whom both eyes fulfil the criteria outlined above In 3 cases the corneal stroma was found to be thicker in the eye with elevated IOP in 4 cases it was thinner and in one case no difference was found The mean value of the differences (0 004 mm) is found not to differ statistically significant from zero (P < 0 4)

Table II shows data for 14 patients with initial IOP *in one eye above 30* mm Hg and a fall to between 10 and 20 mm Hg after treatment The mean value of the thickness differences is found to differ statistically significant from zero (t = 5 15 P < 0 001)

The effect of the given treatment upon the thickness of the stroma has been studied by giving the same treatment to a group of volonteers (Table III) A small reduction in IOP was seen and no effect upon thickness In 4 cases the thickness was smaller after the treatment in 3 cases it was greater and in 2 cases identical values were found before and after treatment for 48 hours The mean of the differences is found not to differ statistically significant from zero (P < 0 6)

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A direct parellel to the previous study on reduced IOP (*Ehlers & Riise* 1967) would be a report on a greater number of patients with unilateral non irritative (simple) glaucoma in one eye and a normal contralateral eye These patients are unfortunately seen only seldom Table I includes but 8 patients No significant difference in thickness has been found *Sbordone* (1953) studied the corneal thickness in acute and chronic glaucoma In two cases of acute glaucoma the thickness was increased considerably an observation made several times during the present study In 12 cases of long lasting presssure difference (chronic glaucoma) the cornea of the eye with the higher pressure was thinner in 9 cases and thicker in 3 cases On an average the cornea was thinner in the eye with the higher pressure *Ytteborg & Dohlman* (1965) presented a rather impressive table including 15 cases of IOP of 31 to 68 mm Hg in one eye and normal IOP in the other eye No epithelial oedema was present A comparison of the two mean values showed no significant difference in thickness ($P < 0\ 25$) however by paired comparison a value of $P < 0\ 02$ is found suggesting an increased thickness of the total cornea at increased IOP From studies on the physiology of the cornea (*Maurice & Giardini* 1951 *Honegger* 1962) it is evident that when the endothelial barrier is removed or broken down an increase in stromal thickness occurs This is probably what happens in acute glaucomas and after operations where considerably increased thickness is found However it says nothing about the effect of IOP when an intact endothelium is present In the above mentioned table of *Ytteborg & Dohlman* it is not mentioned whether all cases were non irritative glaucomas neither is it mentioned whether the pressure in any of the contralateral eyes had been reduced by operation *Iuglio* (1967) studied 5 cases at high normal and low IOP The cases are not further characterized and for the reasons mentioned above several interpretations are possible

By comparing the thickness of the stroma of the same cornea at normal and high IOP the data in Table II were found The thickness increased significantly ($P < 0\ 001$) when the IOP was reduced from above 30 mm Hg to the normal range ($10 \leq IOP \leq 20$) The treatment employed to reduce the IOP had no measurable effect upon the thickness (Table III) It therefore appears that the changes in thickness are caused by the changes in IOP The IOP had probably been elevated for a prolonged period of time as no treatment were given the two foregoing days The values at normal IOP were not measured until the pressure had been normalized for 1 or 2 days The uncertainty of not being in a steady state condition when measuring pressure and thickness is therefore probably eliminated It may be concluded that the IOP exerts a reducing effect upon the thickness This agrees with the mentioned *in vitro* experiments on monkey eyes and supports the existence within the physiologic range of me

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MESODERMAL DYSGENESIS OF THE CORNEA AND IRIS (RIEGER S ANOMALY)

Report of a Case

BY

BIRGITTA ZETTERSTRÖM

Mesodermal dysgenesis of the cornea and iris is a developmental anomaly which occurs as early as the seventh month of intra uterine life A hereditary tendency is well established and a vast literature on the condition exists *Herwigh Rieger* (1934 1935) *studied the anomaly extensively and* described the clinical features in more detail It is now generally known as Rieger s anomaly He observed the association of dental anomalies in some cases and later assumed that dental anomalies and the dysgenesis could be connected

The characteristic features of the condition are abnormality in the development of the cornea the angle of the anterior chamber and the anterior stromal layer of the iris whilst the sphincter pupillae and the posterior mesodermal layer of the iris are normally developed Mesodermal remnants span the chamber angle and this may give rise to buphthalmos or infantile glaucoma Anterior synechiae from the iris to the posterior aspect of the corneal periphery may lead to traction on the pupil producing corectopia dyscoria or slit like pupils

Sharf (1941) described 2 cases in which progressive iris atrophy caused a tear in the iris and resulted in glaucoma

The clinical course of mesodermal dysgenesis of the cornea and iris is still obscure Few workers have discussed it (*Starke* 1951 *Kittel* 1956) *Lemmington*

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chanical factors in the maintenance of normal corneal thickness and state of hydration

Summary

The thickness of the corneal stroma has been studied in cases of glaucoma In 8 cases of unilateral glaucoma no difference in thickness could be observed In 14 cases of glaucoma a statistically significant increase in thickness was observed when the intraocular pressure was reduced by medical treatment from above 30 mm Hg to the range 10–20 mm Hg In a control series the treatment had no effect upon the thickness It is concluded that within the physiologic range increased pressure reduces the thickness of the cornea

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& *Riethe* (1958) considered progressive iris atrophy giving rise to partial aniridia to be of great pathological significance The literature however does not contain any case to the best of the author s knowledge in which the anomaly was diagnosed early and the clinical course was followed up for a prolonged period of time

A case of mesodermal dysgenesis of the cornea and iris was seen in this Department in which the anomaly was suspected in the first week of life its presence being confirmed in the seventh month and the clinical course has been followed up for four years at the time of writing This was therefore considered to be sufficiently interesting to be reported

Case Report

The patient was a first child Her weight and height at birth were 3 350 g and 50 cm respectively Her mother aged 32 years had been healthy throughout her pregnancy and was delivered in the fortieth week The patient s father had the same eye disease as she herself otherwise the family history was irrelevant.

Immediately after the birth of the patient both corneae were found to be so opaque that it was impossible to inspect the anterior chambers The cornea was found to blend with the sclera without sharp demarcation at the limbus and a large number of superficial vessels were present in this area Both eyes were white and the cornea did not stain with fluorescein There was no appreciable response to light and the intra ocular pressure was normal

The patient was referred to the Paediatric Unit of this hospital for further investigation The Gonococcal complement fixation test w s negative as was Rubella culture The toxoplasma dye test and the complement fixation test showed -1/10 and -1/7 respectively The test for Listeria was negative The values of serum calcium and alkaline phosphatase were normal Amino acid analysis by paperchromatography revealed no abnormality The blood count was normal the Wasserman reaction was negative and there was no evidence of systemic disease

During the first few weeks after birth the corneal opacity of both eyes gradually receded The intra ocular pressure was normal being 8/5 5 (12 mm) as measured under anaesthesia with a Schiotz tonometer and Goldmann s applanation tonometer for both eyes

At the age of eight months both corneae had become sufficiently translucent to enable some details of the anterior chambers of both eyes to be recognized As had been found at birth the cornea blended with the sclera without any sharp demarcation and there was marked vascularisation of the limbus The pup l margins were only partly visible but the colour of the iris which was bluish grey could be distinguished F liform bands were vis ble extending from the anterior lamina of the iris to be inserted into th e posterior surface of the cornea The corneal opacities however had not yet receded sufficiently for the fundi to be inspected The intra ocular pressure of both eyes w s 1? mm as measured with Goldmann s applanation tonometer

S me details of the anterior chamber which appeared to be malformated were now sufficiently clearly visible to be photographed (Fig 1)

At the age f twenty months both corneae had become st ll more translucent The demarcat on between the cornea and sclera was st ll indistinct and numerous blood vessels resembling superficial vessels in type were still present in this area The

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MALIGNANT MELANOMAS OF THE HUMAN UVEA

Recent Follow up of Cases in Denmark 1943–1952

BY

O A JENSEN

All cases of intra ocular malignant melanomas in Denmark within the ten year period 1943–1952 were personally investigated clinically histopathologically and prognostically and the results published in a monograph in 1963 (14)

The present follow up includes the same cases the observation period now having been extended by a further five years

Material and Methods

As regards collection analysis and the clinical and histopathological aspects of the material reference is made to the above mentioned monograph (14) Each case has now been followed until death or up to the terminal date of the follow up January 1 1966 The shortest observation period has therefore been 13 years and the longest 23 years This was made practicable by the aid of general practitioners the census registers the Danish Cancer Registry the Central Card Index for Deaths of the Danish Health Department and the National Record Office where all death certificates are

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Reprint requests to O A Jensen, Ophthalmic Pathology Laboratory Rigshospitalet Tagens ej 18 00 Copenhagen N Denmark
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Fig 1
The patient s eyes at the age of eight months

entire pupil margin was now visible The intra ocular pressure of both eyes was 14 mm (Fig 2)

At the age of three years and two months the demarcation between the cornea and sclera was more clearly visible and the limbus was found to be less vascular than at the previous examination The pupil was clearly seen The iris which showed markedly atrophic changes in places was clearly outlined Filiform and chord like membranes were seen to stretch from the periphery of the anterior lamina of the iris across the anterior chamber to find insertion into Descemet s membrane The visual acuity of both eyes was 5/20 The cornea was 9 5 × 10 mm in diameter The intra o ular pressure was 14 mm (Fig 3)

At the age of four years the visual acuity was found to be 5/10 for both eyes Retinoscopy showed the refraction of both eyes to be + 4 00 The fundi could not be clearly distinguished but appeared to be normal The intra ocular pressure was 1? mm (Fig 4)

The number of teeth corresponded to the age of the infant

The gonioscopic appearences was indistinct In places membranous bands were seen to span the angle chamber extending from the anterior lamina of the iris to the poste

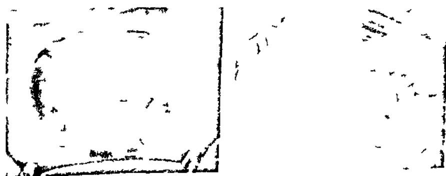


Fig 2
The patient s eyes at the age of twenty months

filed as well as by hospital records and post mortem reports Where autopsy had been performed all available histological material was procured and examined

In this work surviving patients were not examined personally except for a few cases in the Ophthalmic Tumour Centre at the Ophthalmic Pathology Laboratory the status of the patients being based on the hospital records and on information from general and ophthalmic practitioners

Some borderline cases were re evaluated with respect to cell type reticulin content and pigment content which explains small differences of the figures in some tables compared with the same tables of the previous publication

The data collected were analysed by the K H system (14) The distributions were compared using the χ^2 test

The table numbers in squared brackets refer to tables in the previous publication (14) for the sake of comparison Table numbers and numbers in parentheses refer to the present publication.

Results

A survey of the follow up can be seen in Table 1 [Table 39] The same number of patients as previously could be traced so that a follow up percentage of 99 was obtained 72 per cent of the total number being dead at the time of follow up Further reference to the single groups in Table 1 will be made below The cases of iris melanoma will be dealt with separately at the end

Follow-up of survivors (Choroid and ciliary body tumours) (see Table 1) Regarding the two patients alive with previous orbital recurrence reference is made to Table 2 below (case Nos 260 and 266) These patients are the same as those in [Table 39]

The patient alive with metastasis (case No 231) showed signs of this 13 years after enucleation The primary tumour of the mixed cell type had invaded the sclera slightly By explorative laparotomy a melanoma metastasis in the omentum was found and totally extirpated The patient was healthy at the time of follow up but died later with metastases present The two patients alive with signs of metastases in the previous table [Table 39] died shortly after the previous follow up

Follow up of dead (Choroid and ciliary body tumours)

From Table 1 it can be seen that half of the 214 dead patients died in hospital and half at home Of the latter about half had been in hospital shortly before death In 154 of the cases (53 per cent) the patients died with metastases present In about two fifths (38 5 per cent) of these the metastases were verified by autopsy or premortal biopsy and in a further 6 per cent by explorative laparotomy without histological verification The rest died with metastases present according to death certificate The overall autopsy frequency of the material was 31 per cent



Fig 3
The patient s eyes at the age of three years and two months Visual acuity was bilaterally 5/20



Fig 4
The patient s eyes at the age of four years Visual acuity was bilaterally 5/10

rior aspect of the cornea. Fine details could not be distinguished The angle of the chambe was open and of average width

The eyes of the infant s father aged 37 years were examined and photographed (*Fig* 5) Demarcation between the cornea and sclera was indist nct and fibres were seen to exten l from the iris to Descemet s membrane in places The lenses were clear and the fundi d d not show any abnormality The corneae were 10 × 10 mm in dia meter The visual acuity of the right eye was 0 2 (+ 7 00) th..t of the left being 0 4 (+ 7 5) The *intra ocular* pressure were 8/5 5 Schiotz There was no evidence of dental anom lies

The maternal and paternal grandparents as well as their brothers and sisters and the children of the latter had no known eye disease

The patient s father stated that his sight had improved since childhood As he had not been ophthalmologically examined until adult age objective infor

Table 1
Survey of follow up

	Chor	Cil body	Chor + cil body		Iris	Uvea	
	Number	Number	Number	%	Number	Number	%
Followed up	281	11	292	99	10	302	99
Not followed up	3	–	3	1	–	3	1
Alive no signs of metast	71	4	75		7	82	
Alive w excised orbital recur	2	–	2		–	2	
Alive w signs of metast	1	–	1		–	1	
Total alive	74	4	78	27	7	85	28
Died at home	107	1	108		1	109	
Died in hospital	104	2	106		2	108	
Total dead	211	3	214	73	3	217	72

Orbital recurrence

A survey of these cases can be seen in Table 2 [Table 43] Intra ocular biopsy was performed in 12 cases of the whole series Among these were one case of orbital recurrence two of latent tumour cells (16) and one case of benign post operative conjunctival melanosis

In the rest of the material of choroidal and ciliary body melanomas without biopsy (280 cases) seven cases of orbital recurrence were found i e 2 5 per cent No new local recurrence had come to light since the previous record One patient (case No 243) with a recurrence of latent tumour cells in the orbit 24 months after enucleation had died from other cause 12 years after enucleation without further local recurrence or metastases The orbital recurrence appeared in the present series at an average of 2 years after the primary operation

Regarding therapy of the local recurrence in the present series exenteration of the orbit was performed in two cases excision of the recurrence in five In two of these a second recurrence required orbital exenteration The two patients with latent tumour cells *had their recurrences excised Both had died 3 years*



Fig 5
The eyes of the patient s father aged 37 years Visual acuity of the right eye was 0 2 that of the left being 0 4

mation about this point was lacking Fig 5 shows the eyes of the patient s father

This case is of special interest inasmuch as the clinical course of the anomaly has been followed up for four years at the time of writing There was photo graphic evidence of regression of the opacity of the corneae concurrently the pathological changes in the anterior chamber became visible and there was ob jective evidence of improvement of vision

Summary

A case of mesodermal dysgenesis of the cornea and iris is reported in which the anomaly was suspected in the first week of life its presence being confirmed in the seventh month and the clinical course of the condition has been followed up for four years at the time of writing

Interesting features of the case were that the bilateral congenital opacity cleared sufficiently for details of the anterior chamber to be photographed and that there was objective evidence of improvement of vision

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Table 2

Survey of cases with orbital recurrence in the present series

Case No	Du f p st hist	Primary operat n	Intra oc lar b psy	Size (mm) of prima y tum	Scle al inv sion	E trascleral e tens n	Invasion f optic d sc	Inva ion f optic n ve	Cell typ f prima y tum r	F bre g p (p m t)	L c l ft p p	S cu n ft p p
6	1 mths	En cl	–	60	+	+	–	–	M xed predom. spindle B	Absent	10 mths	
75	36 mths	Enucl + partial exent f orbit	–	D ffuse uveal growth	+	+	–	+	M xed predom ep th	M ked	4 5 mth	
118	18 mths	En l	–	52	+	–	–	–	Mi ed q ally sp ndle and p	?	14 mths	
1	11 days	Enucl	–	?	?	?	?	?	?	?	6 yrs.	8–9 yrs.
183	8 d ys	En cl	–	91	+	+	+	–	Ep th	Absent	5–6 yrs	6 yrs.
215	0 y s ? 2 mths ?	E ucl	–	132	+	+	+	–	M xed q ally sp a d p th	L ght	9 mths	
243	1 mth	Enucl	P eoper at vely	90	+	–	–	–	Sp ndle B	L ght	4 mths	–
58	4 mths	Enucl	P cope at ly	?	?	?	?	?	M x d	?	18 mths	
60	10 days	Enucl	2 days bef e op	40	–	–	–	–	Sp ndl B	M d um	6 yrs	–
66	1 mth	E u l		?	+	–	+	–	Ep th	?	8 mths	

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ON CORNEAL THICKNESS AND INTRAOCULAR PRESSURE II

A clinical study on the thickness of the corneal stroma in glaucomatous eyes

BY

NIELS EHLERS

In a previous study (*Ehlers & Riise* 1967) it was demonstrated in a group of patients with unilateral retinal detachment that when the intraocular pressure (IOP) was low the corneal thickness was greater than in the contralateral normotensive eye This observation was in agreement with *in vitro* experiments on monkey eyes (*Ehlers* 1966 1967) showing that the IOP exerts a reducing effect on the swelling of the cornea The *in vitro* experiments further suggested that a reduced thickness of the corneal stroma should be found in eyes with elevated IOP

Only few reports on the correlation between corneal thickness and increased IOP exist (*Sbordone* 1953 *Ytteborg & Dohlman* 1965 *Iuglio* 1967) and the results are contradictory

The purpose of the present study has been to compare values for the thicknes of the corneal stroma in eyes with high IOP with 1) the thickness of the stroma in the contralateral normotensive eyes and 2) the thickness of the stroma in the same eyes after the IOP has been normalized by medical treatment

Methods

Patient material All patients included in this study suffered from non operated glaucoma had good central vision and clinically normal corneas especially no epithelial oedema Patients admitted to the Eye Department for glaucoma were

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Table 2 (cont.)

Extent. of orb.	Ep th.				16 mth	6 mths		3 mth	1 mths.		D th t f t
Exent. of rb	Mix d, p d m. ep th		33 y					1 mths.	8 mth		D th c rt.
X ys					14 mth	At th same t m		20 mths.	6 mth		D th rt
Extirp. Exent. of orb.	Mix d, q ally p and ep th.	Mi d, p ed m. ep h			10 y	14 y 18 mth	M d p d m. p dl A	10 y	4–5 yrs.	18 mths.	A t p y
X rays Exent. of orb		Ep th.			9 y	24 mths. 21 mths.		9 y s.	6 mths.	2 yrs.	Lap t my
X rays								14 mth	4 mth		D ath rt.
Extirp	Lat nt p dl B			10 yrs.				12 yrs.	10 yrs		D th rt.
Extirp	Latent m ed. pred m ep th.		Absent		34 mths.	15 mths.		3 y s.	18 mth		A t p y
Extirp	M d		Ab t	15 yrs.							
Ex rp				15 yrs.							

informed not to treat the glaucoma on the day of admission and the day before. As a result a number of patients showed elevated IOP. The thickness of the corneal stroma was measured and compared with the thickness in the contralateral eye if this showed normal IOP (Table I) and with the thickness in the same eye after the IOP had been reduced by treatment with pilocarpine, acetazolamide and in some cases adrenaline if the contralateral eye could not be used for comparison (Table II). In order to rule out an effect of the given medical treatment on the thickness of the corneal stroma a control group of persons with normal IOP was included (Table III).

Measuring technique. The corneal thickness was measured according to the principle of Jaeger using the attachment I to the Haag Streit slit lamp. This apparatus appears to be the most reliable at the present time (*Honegger & Genee* 1968). The procedure followed has previously been reported (*Ehlers & Riise* 1967). Although cases showing epithelial oedema have been excluded a subclinical oedema might increase epithelial thickness. For this reason only the stromal thickness was measured as illustrated in Fig. 1.

The results have been statistically evaluated by paired comparison using the t test as corneal thickness was found not to differ statistically significant from the normal distribution (*Kruse Hansen* to be published). In tables II and III only one eye from each patient have been included in order to have statistically independent data.

Table I

Corneal thickness in cases of unilateral glaucoma

		Glaucomatous eye		Contralateral eye		ΔT (μ)
		IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
KH	f	60	488	21	484	– 4
EL	m	32	478	17	478	0
MJ	f	38	480	20	492	12
EM	f	70	426	17	444	18
KF	m	38	440	16	436	– 4
CM	f	32	410	10	398	–12
AT	f	62	458	10	464	6
TJ	f	50	460	16	476	16
mean		48	455 ± 10	16	459 ± 11	4 ± 4

The table show corresponding and simultaneous values of IOP and thickness of corneal stroma in patients with unilateral glaucoma. Lower line mean ± standard error of mean.

Table 2

Survey of cases with orbital recurrence in the present series

Case No	Dur f past h st	Pr m ry ope at on	Intra ocular b opsy	Si e (mm) of primary tum	Scler l invasion	Ext ascle al ext ns n	Invas on of opt c d sc	Invas n of pt c nerv	Cell type of pr m y t m r	F bre g up (p m t)	L l e ft p p	S
6	1 mths	Enucl	–	60	+	+	–	–	Mixed pred n sp ndle B	Absent	10 mths	
5	6 mth	Enucl + pa t al xent of o b t	–	D ff e uveal growth	+	+	–	+	M xed pred m p th	Marked	4–5 mths	
118	18 mths	Enucl	–	52	+	–	–	–	M xed equally sp ndle and ep	?	14 mth	
1 ?	11 days	Enucl	–	?	?	?	?	?	?	?	6 y s	8–9 yrs.
183	8 days	En cl	–	1	+	+	+	–	Ep th	Ab nt	5–6 yrs.	6 yrs.
15	0 yrs.? mths ?	En cl	–	132	+	+	+	–	M ed q ally p and ep th	L ght	9 mths	
243	1 mth	Enucl	Pre p r at ely	90	+	–	–	–	Sp ndle B	L ght	4 mths.	–
58	4 mth	Enu l	P oper at vely	?		?	?	?	M ed	?	18 mths	–
r60	10 days	E cl	2 days bef e op	40	–	–	–	–	Sp dle B	Med m	6 yrs	
66	1 mth	Enucl	–	?	+	–	+		Ep th	?	8 mths	–

Table II

Effect of reduction of elevated IOP upon thicknes of corneal stroma

			Before treatment		After treatment		ΔT (μ)
			IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
ND	m	os	56	446	29	482	36
OS	m	os	48	404	19	434	30
MJ	f	os	48	426	18	460	34
AT	f	os	62	458	12	500	42
PB	m	od	44	432	15	438	6
HK	m	od	38	448	18	480	32
AV	m	od	32	452	17	452	0
MN	f	od	37	448	19	478	30
AP	f	os	39	464	16	468	4
HS	m	od	35	454	20	466	12
AM	m	od	32	438	17	472	34
EJ	f	os	34	458	20	468	10
TP	m	od	35	426	12	436	10
MC	f	os	30	434	20	438	4
mean			49	442 ± 4	18	462 ± 5	20 ± 4

The table shows corresponding values of IOP and thickness of corneal stroma in eyes at high (IOP ≧ 30 mmHg) and normal (20 ≧ IOP ≧ 10 mmHg) intraocular pressure The pressure was reduced by treatment with pilocarpine acetazolamide and adrenaline Lower line mean ± standard error of mean

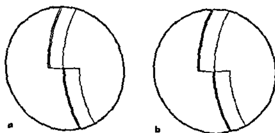


Fig 1

In the corneal microscope the endothelium appears single contoured The epithelium however shows a definite thickness and it is therefore possible to measure total thickness (a) or as in the present study only stromal thickness (b)

Table 2 (cont.)

T E	C ll typ f	C ll typ f	F b ( )	Al (ft p p)	M t (ft p p)	M t (ft loc ct)	Cell typ f t	De (ft)	D d (ft)	De d (ft)	(f nfc (t d)
Extent of orb	Ep th.				16 mths	6 mth		23 mths	1 mth		D th rt f t
E nt. f b	M d, P dom ep h		H y					12 mths.	8 mth		D th rt
X y					14 mth	At th m t m		0 mths.	6 mths.		D th rt
E t rp 2) Ex nt. f orb.	M d, qually p d p h	M d, p d m p th			10 yrs	1) 4 yrs 2) 18 mths.	M d, p d m. P dl A	10 y	4–5 yrs	15 mth	A t psy
1) X y 2) Ex t of b		Ep b			9 y	1) 24 mths 1) 21 mths		9 y	6 mth	2 yrs.	Lap t my
X ray								14 mth	4 mth		D th rt.
Ex p	Lat t p dl B			10 y				12 y	10 yrs		D th rt
Ext p	Lat t m d p d m p h		Abs t		34 m h	15 mth		5 yrs.	18 m hs.		A t psy
E t rp	M d		Absent	15 y							
Ex rp				15 yrs.							

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DENDRITIC (HERPETIC) KERATITIS

I. Incidence – Seasonal Variations – Recurrence Rate – Visual Impairment – Therapy

BY

M. S. NORN

Herpetic keratitis is a frequent disease often causing lost working days. The disease represents a steadily increasing problem within our highly advanced social system where other diseases are combated with greater success.

The present possibility of instituting rational treatment with 5-iodo-2-deoxyuridine (IDU), which interferes direct with the viral metabolism, is regarded as a great improvement.

Numerous reports have been published on this subject since *Kaufman et al.* (1962) introduced IDU treatment against dendritic keratitis. A favourable result has been noticed in most cases (*Kaufman, Anseth et al., Capperucci, Mach et al., Laibson et al., Maxwell, Patterson et al., Sood et al.*, etc.).

The response to IDU has been studied through double-blind trials, using as placebo water or substances of at least doubtful therapeutic value.

These trials have shown IDU to give more rapid cure than placebo (*Patterson, Laibson, Jepson, Hart et al., Davidson, Burns*).

Ey et al. and *Mackenzie* took up a more reserved attitude. The latter found carbolisation to have a better effect than IDU. *Gilkes* found no significant difference between the effects of iodine cauterisation and IDU therapy.

Some workers state that a favourable response to IDU is only obtainable

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and 12 years respectively after the enucleation or 18 months and 10 years after the recurrence

Disregarding the last mentioned two cases death occurred at an average of 19 months after the orbital recurrence or about 4 years after enucleation

Prognosis

This is estimated on various clinical and histopathological features in a group of 230 cases each followed up 15 years after the enucleation

The prognosis in relation to sex and age can be seen in Table 3 [Table 49] As was previously found the prognosis for men is independent of age whereas women below the age of 40 seem to have a better prognosis than women above that age

The prognosis in relation to size is recorded in Table 4 [Table 52] A com

Table 3
Prognosis in relation to sex and age (15 year obs period)

Age	Males				Females			
	Alive	Dead		Total	Alive	Dead		Total
		metast	*other* cause			metast	other cause	
0– 9	1	–	–	1	–	–	–	–
10–19	1	–	–	1	–	–	–	–
20–29	–	1	–	1	3	1	–	4
30–39	10	4	–	14	5	1	2	8
40–49	12	16	–	28	7	12	1	20
50–59	11	21	1	33	6	20	3	29
60–69	7	20	12	39	7	10	3	20
70–79	2	7	7	16	–	5	6	11
80–89	–	–	–	–	–	3	2	5
Total	44 33 %	69 52 %	20 15 %	133 100 %	28 29 %	52 54 %	17 17 %	97 100 %
	5 % < p				0 1 % < p < 1 % for < 40 yrs			

(Testing based on the age groups < 40 yrs 40–60 yrs and > 60 yrs The groups of alive and died from other cause have been combined)

haemorrhages Profuse retinal haemorrhages have been observed only in a few cases (*Dow* 1965 *Quock & Donohoe* 1967)

Since the introduction of a clinically applicable method of fluorescence angiography (*Novotny & Alvis 1961*) this procedure has been widely used for investigation of the retinal and choroidal circulations (*Shikano & Shimizu* 1968 *Wessing* 1968, *Rosen* 1969) In Eales disease leakage of fluorescein from the diseased vein has been consistently observed According to *Shikano & Shimizu* the fluorescein pattern is due to factors such as diffuse leakage of dye from arterioles and capillaries resulting in the formation of multiple irregular fluorescent spots and retention of dye in the affected vein wall

The present paper describes the appearance of retinal vascular lesions as revealed by fluorescence angiography in a case of sarcoidosis

Method

With the patient in a sitting posture the pupil is dilated with Mydriacyl® (Alcon Lab) and a 10 per cent solution of sodium fluorescein is injected into an ante cubital vein

The Zeiss fundus camera equipped with an automatic film changer (Robot motor recorder) is used The fluorescence excitation filter is a blue filter (Schott BG 12) which is placed in front of the xenon flash tube The barrier filter (Schott GG 14) is placed in front of the film This filter transmits light of wave lengths of about 490 nm and longer *i e* 15 per cent of the light is transmitted at 490 nm and 85 per cent at 530 nm The power source for the xenon flash tube is the Zeiss Siemens flash generator

Case Report

The patient a woman aged 35 years had several episodes of otitis in childhood but otherwise had enjoyed good health until she developed pain in the lower half of the thorax She was admitted to the Lung Clinic St Gorans Hospital Stockholm where the diagnosis of sarcoidosis (uveo parotid fever) was made

X ray of the lungs disclosed bilateral hilar lymphadenopathy and at a later stage a fine disseminated mottling in the parenchyma Both parotid glands were enlarged but there was no evidence of sialolithiasis or septic parotitis

A few weeks after her admission ophthalmological examination revealed anterior uveitis in the left eye and two months later in the right After a further four weeks the bilateral anterior uveitis was found to have progressed and there was evidence of involvement of both fundi Concurrently the patient developed a peripheral facial paralysis on the left side (Bell s palsy) and mild lagophthalmos as a sequel About six

Table 4

Prognosis in relation to size (15 year obs period)

mm²	Alive	%	Dead (metast)	%	Dead (other cause)	%	Total	%
< 100	53	*40*	55	42	24	*18*	132	*100*
> 100	16	*20*	51	65	12	*15*	79	*100*
Not determinable	3		15		1		19	
Total	72		121		37		230	

0.1% < p < 1% (In testing the groups of alive and died from other cause have been combined)

parison has been drawn between patients with primary tumours of 100 mm² or less and tumours exceeding 100 mm² at the time of enucleation Measurement in only two dimensions was possible in the present series The analysis shows that the prognosis is significantly worse in cases of tumours with an area of more than 100 mm² No significant difference was found in using any other groupings The prognosis in relation to scleral invasion and extrascleral extension can be seen in Table 5 [Table 53]

In both cases the prognosis appears to be worse when invasion and especially extrascleral extension was found in the enucleated eyeball In cases of invasion of the optic disc the optic nerve and the retina no significant increased lethality was found

The *prognosis in relation to cell type can be seen in* Table 6 [Table 54] *The* classification of the tumours is according to Callender (7) The table also records the prognosis in the whole series It can be seen that 53 per cent had died with metastases present over a 15 year observation period and that the lethality of the epithelioid group is two and a half times as high as in the spindle B group It can also be seen that after revision only a few tumours in our series could be classified as spindle A or fascicular

Fig 1 illustrates the actuarial survival curves for melanoma cases of the different cell types In these curves the spindle types are grouped together and the few fascicular cases left out It can be seen that spindle cell tumours yield an 80 per cent chance of survival five years after enucleation whereas only about 30 per cent of patients with the epithelioid type have a chance of survival The malignancy of the epithelioid tumours is also illustrated by the fact that more than half the patients with this tumour die with metastases present within

months later the anterior uveitis was found to have regressed During that time the patient had a short episode of dizziness which was accompanied by a tendency to fall to the left

Laboratory findings The sedimentation rate ranged between 10 and 15 mm/hour The blood count was normal and routine urinalysis did not reveal any abnormality The Mantoux test was positive but direct microscopy guinea pig inoculation and culture in Lowenstein s medium failed to reveal tubercle bacilli in the sputum and gastric juice Serum calcium was 10 6 mg% the urinary calcium level was 17 4 mg% this corresponded to a urinary calcium output of 0.5 g per twenty four hours Liver tests sternal puncture, retromandibular biopsy of a lymphatic gland the toxoplasma dye test and the complement fixation test were negative The Kveim test was positive

The patient was given prednisolone per os Initially she received a dose of 10 mg × 4 per day This dose was gradually reduced to 5 mg × 2 daily but was again increased if required Eye drops of mydriatics and corticosteroid preparations were used

Ocular manifestations There was mild bilateral anterior uveitis with slight ciliary injection and aqueous flare cells were present in the anterior chamber and there were multiple keratic precipitates on the corneal endothelium There were no posterior synechiae but there was evidence of inflammatory deposits in the chamber angle An inflammatory reaction in the vitreous body occurred on several occasions

Two months after the diagnosis of iridocyclitis had been made both fundi howed disseminated haemorrhages and multiple perivascular lesions In the right fundus small fresh haemorrhages involved the areas above the optic disc and between its main ascending branches of the blood vessels some of these haemorrhages became confluent and associated exudates appeared (Fig 1A) Smaller haemorrhages involved the left fundus

Both the retinal arterioles and venules showed changes In the upper part of the right fundus the haemorrhages were soon absorbed Where this had occurred a vein branch was seen to be occluded At ophthalmoscopy an arteriole running adjacent to the latter appeared to be almost completely occluded (Fig 1B) Newly formed blood vess ls originated from the occluded vessels forming a fan like pattern in the retina Several dilated and tortuous branches of the venules joined and opened into a main branch In other areas a few small exu dates and haemorrhages adjacent to the arterioles were present

There were numerous phlebitic lesions (Fig 2) These included segmental sheathing and thickening of the vessel wall in places The blood column of some vessels was considerably narrowed that of others being not visible at all Peri vascular exudates were seen

About one year after the appearance of the ocular symptoms the patient de veloped bilateral secondary glaucoma and oedema of the right optic disc The iridocyclitis and the changes in the chest persisted

Findings at fluorescence angiography In the arterial phase the arterioles were clearly outlined as far as the occluded portion of the vessels in the right fundus

Table 5

Prognosis in relation to scleral invasion and extrascleral extension (15 year obs period)

	Alive	%	Dead (metast)	%	Dead (other cause)	%	Total	%	p
− scleral inv	32	*32*	46	*45*	23	*23*	101	*100*	1 % < p < 5 %
+ scleral inv	22	*18*	76	*63*	23	*19*	121	*100*	
− extrascl extension	51	*28*	92	*51*	38	*21*	181	*100*	0 1 % < p < 1 %
+ extrascl extension	3	*7*	30	*73*	8	*20*	41	*100*	

(In testing the groups of alive and died from other cause have been combined)

Table 6

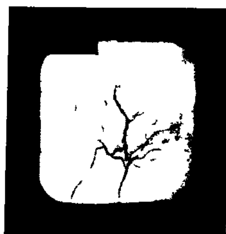
Prognosis in relation to cell type (15 year obs period)

Cell type	Alive		Dead (metast)		Dead (other cause)		Total	
	Number	%	Number	%	Number	%	Number	%
Spindle A	6		1		2		9	
Spindle B	39	*53*	24	*32*	11	*15*	74	*100*
Mixed	23	*21*	69	*62*	19	*17*	111	*100*
Epithelioid	2	*8*	21	*81*	3	*11*	26	*100*
Fascicular	2		4		2		8	
Not determined			2				2	
Total	72	*31*	121	*53*	37	*16*	230	*100*

p < 0 1 % (In testing the spindle cell types have been grouped together and the fascicular excluded In addition the groups of alive and died from other cause have been combined)

two years while half the patients with tumours of the mixed cell type do not die until five years after enucleation The curve for the spindle cell types falls


1 a


1 b


2 a


2 b

Fig 1A

Photograph of the right fundus taken on 6th February 1969 Haemorrhages and exudates are visible above the optic disc

Fig 1B

Photograph of the right fundus taken on 23rd December 1969 A venous occlusion an arteriolar lesion (?) and neovascularization are seen situated above the haemorrhages shown in Fig A

Fig 2

Photograph of the right (A) and left (B) fundus taken on 6th February 1969 Phlebitic lesions of the main lower venous branches are visible Segmental sheathing of the vessel wall obscures the blood column. Small perivascular haemorrhages and exudates are seen

and did not show any other abnormality After the fluorescein had reached the arteriole which appeared to be almost completely occluded at ophthalmo scopy (Fig 1B) the newly formed vessels filled immediately (Fig 4) They dif

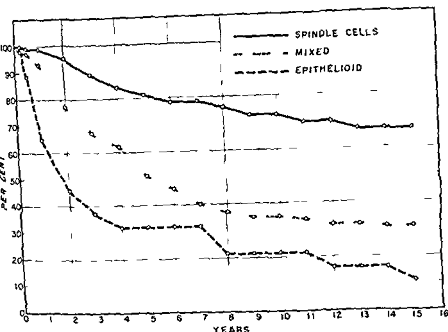


Fig 1

Actuarial survival curves for malignant melanomas of the choroid and ciliary body by cell type based on 230 cases

slowly at first whereas those for the mixed and epithelioid types fall more steeply After about seven or eight years the three curves run approximately horizontally indicating that the chance of dying with metastases after this term of years is small for all patients regardless of the cell type of their tumour The present new follow up shows however that dying with metastases still takes place within all groups of tumour

Prognosis in relation to pigment content can be seen in Table 7 [Table 56] and the corresponding survival curves in Fig 2 The testing showed that the prognosis appears to be better for patients with tumours poor in pigment than for those heavily pigmented

Where the reticulin content is concerned no significant difference in prognosis could be found between patients having had tumours rich in reticulin and those with a poor content It must be stressed that some of the examined material was rather old which might have influenced the result of the reticulum staining

Iris melanomas The ten cases of iris melanoma in seven males and three females of which one was a ι year old girl showed unchanged results at the recent follow up Three had died of whom only one with metastases present

fered in shape and calibre forming a fan like pattern and appeared to originate from this arteriole After filling the newly formed vessels the dye was seen to pass rapidly through the blood retinal barrier and into the retina a large part of which became fluorescent (Figs 3 and 4) The leakage of dye originated from arterioles and capillaries and probably also from venules *The intensity of the fluorescence increased gradually and a few minutes after* injection of the dye fine structural details of the fundus were obscured

An extravascular fluorescent spot which fused with a small haemorrhage was seen in the lower part of left fundus Other fluorescent spots which were not related to large vessels appeared in the early venous phase (Fig 5) These were *probably due to leakage of dye from precapillaries or capillaries* Profuse leakage of dye from the oedematous optic disc was also shown (Fig 4)

From the beginning of the early venous phase until the end of the examination leakage of fluorescein occurred through the part of the vein wall showing segmental sheathing and a broad fluorescent band gradually formed around the vessels (Fig 5) *There was no evidence either of occlusion of the lumina of* veins or of circulatory congestion *in this area* The intensity of the extravascular fluorescence increased the fluorescent band being still clearly visible nine minutes after injection of the dye At that time the individual blood vessels did not contrast with the background the dye being evenly distributed in the tissues

During the following ten weeks the patient was given corticosteroid therapy



Fig 3

Flu escein angi gram of right fundus taken on ?3rd December 1969 Neovascularization and le kage of dye *within* the area of the retina shown in Fig 1B are visible The digits n l ate the interval in seconds between the injection of fluorescein and the taking of the pictures

on a) sex and age b) the size of the tumour c) scleral invasion d) cell type e) pigment content and f) localization in the uvea (iris melanomas)

a) Sex and age Better prognosis for pre menopausal women has also been reported for cutaneous melanomas (5 17 20), and removal of the testes is reported to have improved the condition in a patient with metastases from a malignant choroidal melanoma (13)

Several cases are reported (6 11 18 21 23) where patients with malignant melanomas occurring during pregnancy have a particularly bad prognosis and chloasmata and hyperpigmentation in pregnant women are well known phenomena as also is a fair skin in eunuchs who do not readily become sunburnt These facts indicate some hormonal influence on the melanocytes Some writers however deny a causal correlation between pregnancy and tumour development (6) The exact mechanism of the hormonal influence especially the sex hormonal on melanin production is not known For survey and discussion of the problem reference is made to *Frenkel & Klein* (11)

b) Size The finding by *Flocks et al* (10) that a critical size of the melanoma with a view to the prognosis is about 1000 mm³ is important because it has enabled the clinician to observe the patient with good confidence over a longer period of time so as to become as certain as possible that he is dealing with a malignant neoplasm Many unnecessary enucleations can be avoided when this attitude towards neoplasm suspicious intra ocular processes is followed As previously reported (15) our series shows a better prognosis for tumours of less than 100 mm and if this area can be correlated to a volume of 1000 mm³ which I think is reasonable the Danish material is co incident with the American

The above mentioned writers (10) found small tumours usually to be pure spindle cell tumours and attribute the favourable prognosis to this cytologic characteristic (see below) An analysis of the present series in relation to this correlation showed no significant difference On the other hand an analysis of the material showed that the larger the tumour the greater the tendency to penetration inwards as well as outwards and as can be seen in Table 5 case with scleral invasion and extrascleral extension carry an unfavourable prognosis An analysis of these cases of invasion showed no significant overweight of anaplastic cell types

d) Cell type The prognosis of the individual case is dependent upon many single factors which have to be evaluated as a whole The cell type is probably the best single parameter As found in the previous follow up and in much other material tumours consisting of spindle cells have a much better prognosis than the anaplastic types Our material of the fascicular type is so small that it is not possible to compare the prognosis of cases of this cell type with the prognosis of those of the spindle B type *Zimmerman* (24 25) grouped these types together prognostically Our feeling ha previously been that the fascicular type carried a less favourable prognosis than the spindle B cell type However no further

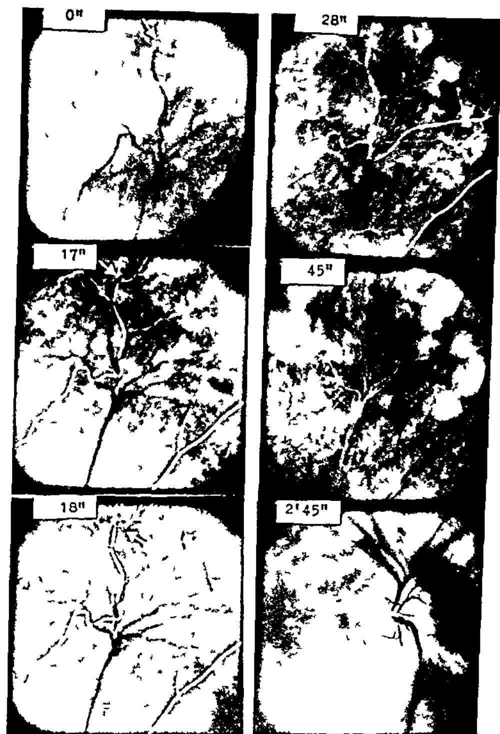


Fig 4

Fluorescein angiogram of the upper part of right fundus taken on 20th February 1970 *i e* two months later than those shown in Fig 3 Arrow points towards a venous occlusion and an affection of an arteriole (?) 18 shows newly formed vessels in the arterial phase Profuse leakage of dye into the retina is visible (cp Fig 3) 2 45 shows the oedematous disc to be brilliantly fluorescent The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures

deaths with metastases present have taken place since the last follow up in this little group of the present series so he may be correct in grouping them together

Zimmerman (25) still groups together tumours of the mixed and the necrotic cell types In our experience necrotic tumours first of all originally belong to the most anaplastic type i e the epithelioid In the present series no tumour was so necrotic that classification was impossible In all cases of nearly total necrosis the remaining cells were epithelioid In our opinion the necrotic group should be omitted from the classification since necrosis is not an adequate histopathological feature for classifying a tumour Further in our opinion it is doubtful whether a classification having more than three groups is justified Morphological classification of most malignant neoplasms ends in a tripartition i e. a differentiated group an anaplastic group and a group in between Our experience (9) concerning the ultrastructure of malignant melanomas strengthens little by little our impression that this tripartition is also a more realistic grouping for malignant choroidal melanomas

e) Pigment content The present analysis again confirms the fact that highly pigmented tumours are the more malignant This was also recently found by *Marquardt* (19) This writer expresses the same surprise as was our experience It was to be expected that melanin production was a highly differentiated characteristic of the melanocyte so that the more pigmented the tumour the more differentiated the cells and the better the prognosis First of all it must be pointed out that dedifferentiation may express a disturbance which affects only one or a few of the many cell functions and if this disturbance affects the melanin production it does not *a priori* mean a decreased production Secondly in my experience much of the pigment seen in the highly pigmented (and malignant) melanomas is lying in melanophages indicating a rapid turn over so that the malignancy might be expressed in loss of a normal inhibition or control of the synthesis According to *Gordon* (12) malignant melanomas may perhaps arise as a result of inhibition of the normal melanocyte development so that mature melanocytes will not be formed On the contrary immature melanoblastic cells characterized by a strong melanin production will be the result

f) Localisation (iris melanomas) The present series showed a significant overweight of tumours localized temporally and posteriorly [Table 21] *Marquardt* (19) found a better prognosis for melanomas with an origin at the equator No difference in prognosis for tumours localized in different parts of the choroid could be found in the present series All choroidal and ciliary body tumours were found to carry the same prognosis The iris however harbours melanomas which differ clinically histopathologically and prognostically from melanomas of the two other parts of the uvea The average age of the present small series was 10 years lower than for the choroidal tumours They were slow growing making the past history long and they were mainly symptomless Only one in

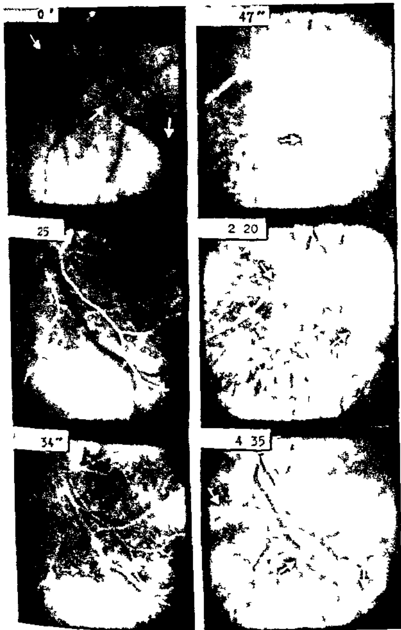


Fig [illegible]

Fluorescein angiogram of left fundus taken on 3rd March 1969 The main lower branches of the retinal veins are visible 0 shows periphlebitic lesions (arrows) 2 20 and 4 35 retention of dye in the inflammatory foci are shown 34 and 47 show a fluorescent spot representing leakage of dye from precapillaries or capillaries (arrows) The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures

ten died with metastases within an observation period of 15 years At the Ophthalmic Tumour Centre we have a very conservative attitude towards iris melanomas During observation it is especially important to notice the size of the tumour its relation to the chamber angle, the appearance of vessels in the iris or on the sclera any darkening of the process or increase of pigment in the chamber angle

If the process is progressing we advise conservative surgery mainly in the form of segmental resection of the iris and ciliary body or iridectomy if the tumour is located centrally near the pupillary margin The long term results of this procedure cannot be determined on the basis of our material at present but large series (4 22) appear to justify this practice The favourable prognosis of the present series was based on enucleation in all ten cases

Conclusion and Summary

In Denmark from 1943 to 1952 a total of 305 malignant uveal melanomas was registered Ten were localized in the iris The average population was 4 1 millions The clinical histopathological and prognostical aspects of this series have previously been published (14)

The present recent follow up deals mainly with the prognosis on a 15 year observation period and with the therapeutic attitude of the Ophthalmic Tumour Centre towards special problems in the management of malignant uveal melanomas At the date of follow up 72 per cent had died The follow up percentage was 99 The frequency of orbital recurrence was 2 5 per cent and 53 per cent of the whole series had died with metastases present based on a 15 year observation period On the basis of experience and the study of the ultrastructure of the tumour a classification of three groups i e a differentiated an anaplastic and a mixed group seems more realistic than the classical Callender classification

The prognosis was estimated in relation to various clinical and histopathological characteristics The prognosis was found to be significantly better for women under the age of 40 for small tumours of less than 100 mm for cases without scleral invasion or extrascleral extension for spindle cell tumours for unpigmented or slightly pigmented tumo and for iris melanomas For the clinician a fundal process of small size a ocation in the iris are particularly useful as both enable him without ri serve the patient over a longer period of time making certain that h aling with a malignant neoplasm Growth of the process and its infl e ne eye are still the only reliable clinical signs of a malignant neopl..s process The prognosis will not deteriorate if the patient is observed until growth is established

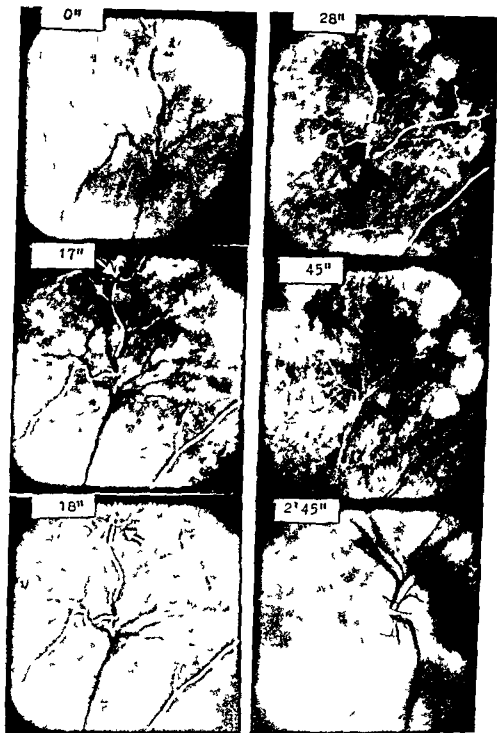


Fig 4

Fluorescein angiogram of the upper part of right fundus taken on 20th February 1970 i e two months later than those shown in Fig 3 Arrow points towards a venous occlusion and an affection of an arteriole (?) 18 shows newly formed vessels in the arterial phase Profuse leakage of dye into the retina is visible (cp Fig 3) 2 45 shows the oedematous disc to be brilliantly fluorescent The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures

This conservative attitude has been practised in the Ophthalmic Tumour Centre since its establishment in 1964 and it is our experience since the enucleated eyeballs are also histopathologically examined by the same team that the 22 per cent of mistaken diagnoses during the years 1943–1952 has decreased considerably probably to below 5 per cent (2)

Modern diagnostic methods such as ultrasonography and fluorescein angiography have of course also contributed to a better diagnosis

Our attitude towards blind and painful eyes especially eyes with intrasparent media, is radical Enucleation is advised since such eyes often harbour a malignant tumour *Exenteration of the eyeball is contra indicated in these cases*

Acknowledgement

The statistics were kindly checked by cand stat Knud West Andersen.

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wall of the veins to be thickened with multiple foci of epithelioid cells and lymphocytes which were arranged in the form of grapes (traubenformig angelagert) *Levitt* (1941) observed the association of retinal periphlebitis and arteritis in sarcoidosis and reported that characteristic features of these cases were mantling of the vessels with sarcoid tissue causing occlusion of the lumina of many vessels or complete replacement of the vessel wall by epithelioid cells According to *Michaels et al* (1960) a similar type of arteritis of the pulmonary blood vessels may be found in sarcoidosis

The case presented in this paper illustrates the typical periphlebitis retinae and the extremely rare arteritis which may be associated with sarcoidosis The arteriolar occlusion appeared to be almost complete as seen in the ophthalmoscope Fluorescein angiography however did not reveal a complete occlusion but showed newly formed vessels originating from this place Fluorescein studies of retinal arteriolar occlusions in hypertension and arterio sclerosis have shown that recanalization of occluded vessels often occurs In the case presented the formation of new vessels suggests that a pathological process had involved arteriolar tissue This process may have been a primary arteriolar sarcoid or it may have been due to the adjacent phlebitis

These types of vascular lesion are highly permeable to fluorescein As most of the dye is bound with serum albumin (*Hodge & Dollery* 1964) plasma proteins and in severe cases probably also blood corpuscles pass through the vessel wall In contrast to normal tissue inflammatory tissue around the vessel wall retains fluorescein The retention of fluorescein in inflammatory tissue has been observed in conditions such as choroiditis Thus the vascular changes revealed by fluorescence angiography in the case discussed correspond to those said to be present in sarcoid vasculitis

As there was no angiographic evidence of choroidal involvement in our case the fundus lesions appear to have been limited to the retina *Shikano & Shimi u* (1968) encountered 3 cases of fundal sarcoidosis in which the retinal circulatory system alone was involved whilst Bruch s membrane and the choroid did not show any abnormality

The clinical and angiographic picture of the vasculitis retinae in the case here presented resembled in many respects those associated with idiopathic perivasculitis (Eales disease) except for the co existent anterior uveitis The high incidence of the association of uveitis and vasculitis retinae was emphasized by *Cross* (1963) The etiology of the retinal lesions may be easily overlooked if the sarcoid iridocyclitis is deficient in characteristic symtoms *Jutte & Lemke* (1966) observed that idiopathic periphlebitic lesions (Eales disease) were highly permeable to fluorescein but considered the blood retinal barrier to be unaffected by the vascular changes which occur in uveitis The observations made in the case presented did not support these findings

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Fluorescein angiography carried out after the completion of this treatment showed that the phlebitic lesions had disappeared *i e* the appearance of the veins were normal (Fig 6) Only a few discrete haemorrhages the venous occlusions and the newly formed vessels were visible in the right fundus

Discussion

Mylius & *Schurmann* (1929) were the first to describe the histological appearance of phlebitic retinal lesions associated with sarcoidosis They found the

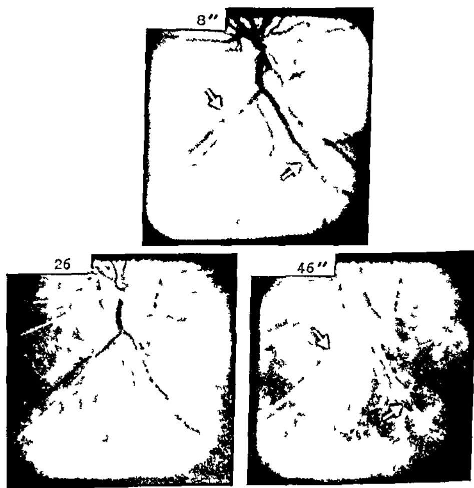


Fig 6

Fluorescein angiogram of the lower part of the left fundus taken on 19th May 1969 *i e* about ten weeks after those shown in Fig 5 There is no evidence of phlebitic lesions (arrows) The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures

From the Department of Ophthalmology
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FLUORESCEIN STUDIES OF RETINAL VASCULITIS IN SARCOIDOSIS

Report of a Case

BY

PEEP ALGVERE

Involvement of the ocular fundus in sarcoidosis probably occurs more frequently than is generally recognized *Geeraets et al* (1962) observed fundus involvement in 40 out of 53 cases of sarcoidosis which they had studied clinically

The most common fundus manifestations of sarcoidosis include perivascular infiltrates resembling candle drippings (*Franceschetti & Babel* 1949) retino choroiditis nodules granulomas and papillitis For a review of these conditions the reader is referred to *Gould & Kaufman* s paper (1961) and Duke Elder s System of Ophthalmology (1966)

von Bahr (1938) was the first to report a case of uveoparotitis associated with sheathing of retinal veins His report was followed by numerous papers on sarcoid involvement of the retinal vessels (*Walsh* 1939 *Meyer* 1939 *Lindau & Lowegren* 1940 *Levitt* 1941 *Wagner* 1941 *Goldberg & Newell* 1944 *Tiong* 1949 *Cross* 1955 *Jutte & Lemke* 1965 *Fontan et al* 1966) These cases usually show perivascular mantling with inflammatory tissue and perivascular distribution of patches of exudate and oedema

Occlusion of the lumen of the vessels may occur and may cause superficial

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Thygeson (1956) found 10 per cent to recover spontaneously while *Laibson* (1964) saw 24 5 per cent to be cured after placebo treatment alone *Burns* found placebo and IDU to be equally effective in the treatment of chronic keratitis or relapses *Davidson* obtained healing of dendritic keratitis in half of his patients within 14 days of instillation of 1 per cent gamma globulin which he himself regarded as a placebo

The immediate success of a treatment (fading of the dendritic pattern and shadowy transformation on IDU treatment and decreasing ciliary congention on steroid treatment) need not indicate a favourable response at the long view

To study the effect of the treatment given I have followed up just over 100 patients to compare the therapy with two of the parametres on which an evaluation of the therapeutic effect on the long view may be based namely the recurrence rate and the visual acuity at the time of the follow up

Present Investigations

The investigation comprised all the patients referred within a seven year period (1958 1964) to the Department of Ophthalmology *Kommunehospitalet* with dendritic keratitis i e a corneal affection presenting a typical dendritic pattern

This characteristic disease was described as early as 1884 by the first professor ophthalmologiae in Denmark *Edmund Hansen Grut* (keratite ramifiee)

No virus cultivation was performed to verify the herpetic affection the morphological picture being generally regarded as sufficiently specific to justify a diagnosis of herpetic keratitis

Incidence

Within the seven year period 157 patients were seen who had had one or more attacks of dendritic keratitis i e 22 4 patients annually

Several of these patients experienced renewed attacks within the seven year period Thus a total of 287 attacks were recorded of which some repeated i e 41 attacks annually

During the same period 6062 patients were admitted to the Ophthalmic Unit while 50270 were treated as out patients Among these a total of 952 had keratitis of some kind or other The recorded cases of dendritic keratitis constituted 1 196 of the total number with ophthalmic diseases

during the first few days of the disease at the subsequent stages IDU hardly does any good (*Jepson Davidson*)

IDU is cytotoxic This explains perhaps the poor effect at the more advanced stages when the virus may be gone and when the epithelial healing does not run a satisfactory course owing to the continued IDU treatment (*Burns*)

Treatment with *steroids* has been extensively discussed and dearly bought experience has been gained from such treatment It is universally agreed that steroid treatment may reduce the resistance of the tissue to bacteria and fungi Steroids may provoke herpetic eruptions Steroids should not be used at the acute stage of herpes

During the subsequent – metaherpetic – phase steroid therapy has been recommended under IDU cover from the view that the metaherpetic phase is due to allergic reaction to the virus in the epithelium Steroid treatment reduces the oedema of the corneal parenchyma thus counteracting cicatrisation and visual impairment

Kaufman (1964) has recommended steroid in cases of geographic ulcer which may follow dendritic keratitis According to Kaufman this ulcer contains no virus actually corresponding to a recurrent erosion Kaufman does not use IDU simultaneously with steroid against geographic ulcer in order not to counteract the tendency to healing

The results of recent investigations suggest however that the herpes virus has not been eliminated at these late stages The virus has been demonstrated in the lacrimal gland (*Kaufman* 1968) the conjunctiva (*Brown Jones Kaufman*) and in the corneal parenchyma (*Dawson et al*) at the clinically inactive stage

Thygeson (1967) warns definitely against steroid therapy owing to his experience regarding a new disease described by him This is termed chronic herpetic kerato uveitis and is a sequela of steroid treated herpetic keratitis The disease persists for years and flares up each time discontinuation of the steroid treatment is attempted

The disease is possibly due to the steroids interfering with the immune mechanism in such a way that the local virus infection of the avascular corneal tissue cannot be brought to a conclusion

A third possibility of treating herpetic keratitis is that of applying *tincture of iodine alcohol phenol or lunar caustic* locally on the process

This treatment is painful but often efficient (*Gundersen*)

The objection may be raised to this therapy that herpes may be activated by a trauma (*Nataf et al*) Such cauterisation is in fact a trauma which may aggravate instead of eliminating the affection

In assessing the various therapeutic possibilities we must not forget that this virus provoked disease tends to spontaneous cure (*Jepson* and others)

The spontaneous course has rarely been studied because the doctor is disinclined to forbear a treatment which may improve an impaired vision

Summary

A case of sarcoidosis associated with pulmonary changes uveoparotitis bilateral anterior uveitis and inflammatory reaction of the vitreous is reported in which the patient developed bilateral vasculitis retinae There was ophthalmoscopic evidence of venous occlusion neovascularization oedema of the optic disc and multiple foci of periphlebitis

Fluorescein angiography revealed profuse leakage of dye from newly formed vessels and the optic disc and retention of dye by perivascular inflammatory infiltrates

The vascular lesions in the case reported resembled those associated with Eales disease

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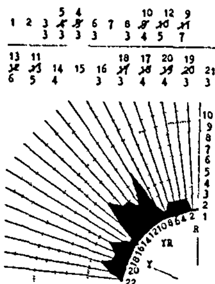


Fig 1
Specimen of Farnsworth Munsell 100 Hue score and profile

of 16 and 35 years (*Lakowski* 1958) After 55 years there is a rapid deterioration in the ability for fine colour discrimination which affects mainly yellow blue or violet blue green discrimination Red green discrimination remains fairly stable and is least affected by age *Verriest* (1963) demonstrated that in normal healthy subjects the error score for the Farnsworth Munsell Hundred Hue test increased in a positive manner with age from the age of 35 onwards At the age of 60 years he quotes a mean error score of 95 with an upper limit of 152 for men

Untreated Tobacco Amblyopia

A group of 65 patients of mean age 67 years was composed of 64 males and one female of whom 57 smoked pipe tobacco only 3 cigarettes only and 5 both The mean tobacco consumption of the group was 3 04 ± 1 44 ozs per week They were diagnosed as suffering from tobacco amblyopia after the criteria of *Heaton et al* (1958) The mean error score for the right eye of all patients for the Farnsworth Munsell Hundred Hue test was 732 ± 236 In an earlier communi cation (*Chisholm* 1969) it was suggested that in the case of error scores above 600 a mean of several test results be taken and below 600 a single test result would be sufficiently reliable Where possible this premise was adhered to A typical 100 Hue profile in untreated tobacco amblyopia shows depressed dis

than those of the Mackay Marg tonometer (MMT) However in comparative studies performed just the opposite was true The MMT – pressure values (P_{MMT}) were as a rule higher than those of the applanation tonometer (P_{AT}) (*Moses et al* 1962 *Hilton et al* 1966 *Tierney et al* 1966 *Suda et al* 1967 *Follmann et al* 1969)

In a more recent study (*Stepanik* 1970) the difference P_{MMT}–P_{AT} proved to be dependent on the level of the intraocular pressure and on the rigidity coefficient of the measured eye and the increase of the intraocular pressure P_0 to P_{MMT} to be equal to a pressure increase produced by a corneal applanation of 4 9 mm in diameter

To elucidate this statement deduced from clinical measurements by calculation, the following experimental study was performed Over a window of a transparent pressure chamber connected to a watermanometer the cornea plus the anterior segment of the sclera of 4 enucleated human eyes was mounted on the slitlamp (Haag Streit Model 900) in such a manner that the cornea could be observed from the inside of the chamber whereas the MMT probe was brought in touch with the cornea from outside (Fig 1) The size of the applanated corneal area was distinctly visible through the cornea in blue light outlined by a fluorescein ring as well as in the optical section. The footplate of the MMT s probe used in this study (Model 200 S/N 4550 Berkeley Tonometer Company California) has a diameter of 4 8 the sensitive area in its center a diameter of 1 6 mm

In this experiment set up it was easy to start the corneal applanation exactly at the center of the probe to dissect the whole recording in sections and record them step by step in correlation to the observed sizes of corneal applanations

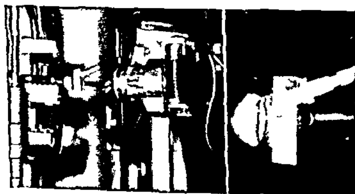


Fig 1

(Stepanik) Experimental set up Transparent pressure chamber and the probe of the Mackay Marg tonometer mounted at the slitlamp of Haag Streit (Model 900)

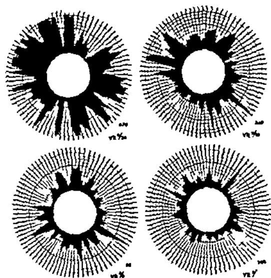


Fig 3

Alteration of Farnsworth Munsell 100 Hue profile with time on treatment with hydro xocobalamin Raw scores and visual acuity are shown in untreated state and after 1 3 and 6 months therapy

We found that when the Farnsworth Munsell Hundred Hue error score was plotted against time on treatment a curve was produced which fitted the expo nential equation $Y = A\ ^{kt} + C$ When such an equation was converted to lo garithms a straight line was produced whose slope was given by the value for k [$\text{Log}_e\ (Y-C) = \text{Log}_e A - kt$] Thus the value for k is an index of the rate of improvement of the patient s colour vision The value for C is the value at which the exponential curve would become horizontal It is an individual cha racteristic dependent on patient age and on the presence or absence of any ocular or systemic disease thought to cause an upset in colour discrimination A computer was used to find the value for C which gave the best fit to indivi dual patient data

To illustrate this the following case may be considered A 68 year old male who smoked 2 5 ozs pipe tobacco per week developed classical tobacco amblyo pia On treatment with hydroxocobalamin he improved Fig 4 shows the Farnsworth Munsell Hundred Hue error score for his right eye plotted against time With a c value of 20 the result of conversion to logarithms is indicated by Fig 5

It is well recognised that patients with tobacco amblyopia show a high inci dence of complicating systemic disease particularly of those diseases associated

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THE MACKAY – MARG TONOMETER

Correlation of the tonogram to the corneal applanations induced by the tonometer

BY

JOSEPH STEPANIK

To eliminate extraneous factors such as rigidity in the corneal tissue to resist deformation and the surface tension of the tears *Mackay & Marg* (1959) devised a new electronic tonometer based on the following principle The plane tip of a small hand held probe carries a pressure sensitive area in its center Current that measures the force on this area is recorded as a function of time on a strip record

Due to *Mackay et al* (1960) the recording reaches the first crest when the flattened cornea is in touch only with the sensitive area The amplitude of this crest indicates the intraocular pressure plus the bending forces of the cornea and thus is the reading that is obtained by the classic applanation tonometers such as that of Goldmann By further increase of the corneal applanation the plate surrounding the sensitive area sustains the bending forces and the sensitive region carries only the intraocular pressure The recorded curve drops therefore to a trough the amplitude of which is a measure of the intraocular pressure

Considering this interpretation of the recording it was to be expected that the readings of Goldmann s applanation tonometer (AT) should range higher

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In 51 patients a definite estimation could be made of the interval in months between the onset of symptoms and seeking medical advice When this was compared with the Farnsworth Munsell Hundred Hue error score a positive relationship was found which was just significant ($r = +0\ 242$ $n = 49$ $0\ 1 > p > 0\ 05$) *Thus poor colour discrimination tended to be associated with* poor visual acuity increased age and a long history of visual symptoms It was found that patients over the age of 65 years sought medical advice within six months of the onset of symptoms as readily as those patients aged 65 years or younger ($x = 0\ 11$ $n = 55$ $p = 0\ 95$) Thus age and tobacco amblyopia play *separate roles in the production of the acquired dyschromatopsia*

In recent years there has been increasing awareness of the part played by avitaminosis B12 in the aetiology of tobacco amblyopia (*Carroll* 1956 *Heaton et al* 1958 *Foulds et al* 1969 *a* and *b*) The serum vitamin B12 of these patients was assayed by the Euglena gracilis method after *Ross* (1952) and a range of concentrations from 15 pg/ml – 5/2 pg/ml with a mean at 196 pg/ml was obtained There was no significant relationship between the serum vitamin B12 concentration and the Farnsworth Munsell Hundred Hue error score in our group of cases ($r = +0\ 161$ $n = 58$ $p > 0\ 1$)

Treated Tobacco Amblyopia

Apart from 5 all the patients were given parenteral vitamin B12 therepy Initially they were given either cyanocobalamin or hydroxocobalamin By observing the improvement in colour vision indicated by a falling 100 Hue error score it was clear that the hydroxocolabamin form of vitamin B12 was superior to the cyanocobalamin form in its therepeutic effect (*Chisholm et al* 1967) All patients therapy was subsequently altered to hydroxiocobalamin at a dose of 1000 μg daily for the first 14 days and then *1000 μg thrice weekly Adjustments* were made dependent on the response Patients were advised that it was not necessary to alter their smoking habit

The improvement in colour discrimination may be observed by studying the change in the Farnsworth Munsell Hundred Hue profile or alteration in the numerical *error score*

A 50 years old male developed classical tobacco amblyopia when smoking 1½ ozs pipe tobacco per week He was treated with hydroxocobalamin and allowed to continue smoking Fig 3 shows his Hundred Hue profile initially and at 1 3 and 6 months after the commencement of treatment There has been a noticeable shrinkage in the areas of error a reduction in the error score and a rise in visual acuity

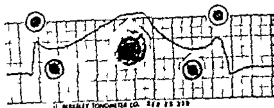


Fig 3
(Stepanik) The regular recording of the Mackay Marg tonometer and the corneal applanations correlated to its crests and troughs

Summary

In the Mackay Marg tonometer using a transparent pressure chamber on the slitlamp the size of the corneal applanations induced by the tonometer at the turning points of the tonogram were observed on 4 enucleated eyes In this study the amplitude of the trough in the ascending part of the tonogram generally accepted as the reading of the intraocular pressure coincided with an applanation of the cornea by the whole footplate area of 4 8 mm in diameter

Acknowledgement

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with deficiency or increased requirement for vitamin B12 In our present group the following diseases were found

Addisonian Pernicious Anaemia	16 9 %
Pre pernicious anaemia (evidence of pernicious anaemia without anaemia)	16 9 %
Diabetes	9 3 %
Hepatic disease	3 1 %
Other conditions	6 1 %
No systemic disease	47 7 %

From the data the following groups of patients were available for comparing rates of improvement in colour vision i e values of k

Croup	Mean value for k
(a) *Tobacco amblyopia with no associated disease treated* by abstinence from tobacco	0 302
(b) Tobacco amblyopia with no associated disease treated by hydroxocobalamin	0 294
(c) Tobacco amblyopia associated with diabetes treated by hydroxocobalamin	0 528
(d) Tobacco amblyopia associated with Addisonian per nicious *anaemia treated by hydroxocobalamin*	0 195
(e) Tobacco amblyopia associated with Pre pernicious *anaemia treated by hydroxocobalamin*	0 341

When the mean slopes for these groups of patients were compared (Fig 6) it was found that the rate of recovery in tobacco amblyopia with no associated disease was as rapid if the patient was treated by abstinence from tobacco as that when treatment with hydroxocobalamin was given and the patient con tinued to smoke* (t = 0 38 p = > 0 1) The rate of recovery in tobacco am

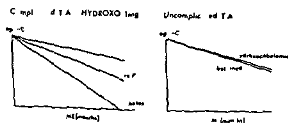


Fig 6
Mean rates of improvement in colour discrimination

(Fig 2) When the fluorescein ring was still within the sensitive area of the probe (a) the record dropped slightly down below the zero line indicating obviously the capillary force of the contact fluid attracting the sensitive area towards the cornea Then the pressurechamber was very slowly moved towards the MMT probe applanating progressively the cornea until the climbing pointer of the tonometer recorder just turned to go down (b) The border of the applanated corneal area was at the inner third of the footplate zone Step c indicates the amplitude of the next turning point of the recorder from going down to going up On that point the cornea was in touch with the whole footplate area the fluorescein ring framing the outer margin of the probe Step d indicates the period of additional indentation of the cornea surrounding the footplate

Pulling now the slitlamp gently backwards step e indicates the amplitude of the recording at the turning point from down to up corresponding to a corneal applanation by the total footplate f indicates the turning point from up to down at a corneal flattening with borders within the inner zone of the footplate and g again capillary traction of the fluid on the sensitive area free of cover *when the fluid ring came in touch with the latter*

Thus in the ascending as well as in the descending part of the MMT recording (Fig 3) the crest corresponds to an applanation of the cornea by the sensitive area plus the inner third the trough to a corneal applanation by the sensitive area plus the whole footplate zone

These experimental data prove therefore in splendid conformity with the results of the foregoing clinical study that the Mackay Marg tonometer does indicate the intraocular pressure at a corneal applanation close or equal to 5 mm in diameter

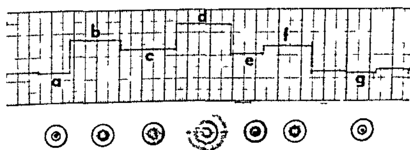


Fig 2

(Stepanik) Step by step registration of the turning points of the Markay Marg tonometers recording and the correlated contact areas of the footplate to the cornea as observed by the slitlamp

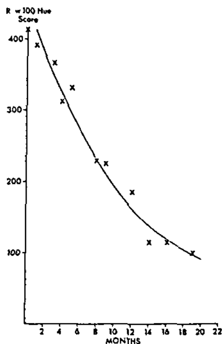


Fig 4

Raw 100 Hue error score plotted against time on treatment

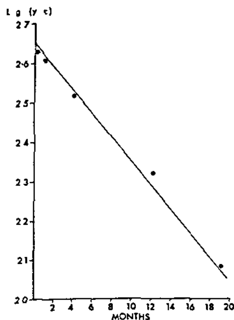


Fig 5

Data of Figure 4 converted to logarithms C value of 20 (r = 0 99)

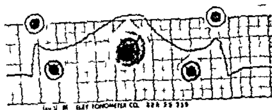


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of the right eye in a patient suffering from classical tobacco amblyopia treated with hydroxocobalamin It is apparent that the visual acuity has returned to normal levels before the ability for colour discrimination It seems probable that the improvement in colour sense is not wholly dependent on visual acuity

Discussion

Defective colour vision acquired by patients born with a potentially normal colour vision system develops through various stages the earliest of which is an abnormal trichromatic stage Pseudo isochromatic plates are of little value in detecting this relatively early stage which however can be picked up by the Farnsworth Munsell Hundred Hue test

Disease processes affecting the neuro sensory or conductive layers of the retina will if severe enough lead to blindness Less severe disease will degrade visual function in a variety of ways including the development of an acquired dyschromatopsia *Thus lesions of the neuro sensory retina* by and large result in a loss of colour discrimination in the yellow blue or violet blue green and lesions *of the conductive layers in the red green areas* of the spectrum respectively (*Koellner* 1912 *Cox* 1960 *Verriest* 1963)

Pigment matching tests of which the Farnsworth Munsell Hundred Hue test is a refined and useful example test the subject s ability to discriminate between colours which differ only by a small amount when viewed under a constant illumination This test enables a qualitative as well as a quantitative estimation of the colour defect to be carried out (*Crone* 1961) One of the great merits of the Farnsworth Munsell Hundred Hue test is that elements suitable for detecting colour confusion can also be used for detecting the variations in colour discrimination existing among trichromatic observers To be able to measure these variations the tasks presented for discrimination must involve small colour *differences such as are found in the Farnsworth Munsell Hundred Hue* test The differences between successive caps is of the order 2 5 N B S units The task here may be considered analogous to visual acuity *testing Subjects* with acute colour discrimination will arrange the colour series in each box within the two end limits correctly those with lesser *discrimination will accu*mulate error scores which are a measure of the degree of displacement from the ideal arrangement (*Lakowski* 1968)

Cale owski (1883) was first to draw attention to the subjective colour defect of tobacco amblyopia and *Groenouw* (1892) pointed out that this acquired *dyschromatopsia differed* from that of the congenital dichromat *Cox* (1960) *François & Verriest* (1961) *Saraux et al* (1966) *Bouniq & Coscas* (1966) all record profiles showing defective red *green discrimination in* Tobacco Amblyo-

Stepanık J Das Mackay Marg Tonometer I Klınısche Studıen A v Graefe s Arch klın exp Ophthal *180* 104 (1970)

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blyopia associated with diabetes was more rapid than when tobacco amblyopia was associated with Addisonian pernicious anaemia* ($t = 2.45$ $p = 0.05$)

The outlook for good visual recovery was as good in tobacco amblyopia unassociated with systemic disease and treated by hydroxocobalamin as in tobacco amblyopia associated with diabetes and treated by hydroxocobalamin* ($t = 0.80$ $p = > 0.1$) The rate of recovery of colour discrimination was slower in those patients whose tobacco amblyopia was associated with evidence of pernicious anaemia than in any other group The mean period of treatment with hydroxocobalamin at full dosage of these patients was 20.4 months before a good standard of vision was achieved This is prolonged when compared with the mean of 6.82 months of those patients with tobacco amblyopia unassociated with systemic disease Of the 65 patients 6 were experiencing a recurrence of the disease and of these 3 had pernicious anaemia It is possible that these patients had never fully recovered from their previous bout of tobacco amblyopia which had been treated by abstinence from tobacco In each of these cases the recurrence had occurred after an interval of not less than 7 years

(* Fractional weighted "t" test)

We have found tests of Hue discrimination a more sensitive indicator of visual improvement than visual acuity and confirm *Riddell's* (1936) findings that the return of colour vision takes longer than the central visual acuity Fig 7 illustrates the rate of visual improvement and recovery of colour discrimination

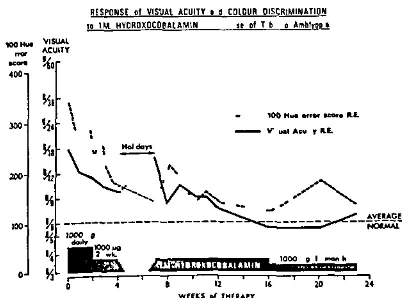


Fig 7

Plot of visual acuity and Farnsworth Munsell 100 Hue with time on treatment illustrating the disproportion between *rate of visual and colour discrimination improvement*

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COLOUR VISION IN TOBACCO AMBLYOPIA

BY

I A. CHISHOLM J BRONTE STEWART and
E O AWDUCHE

One of the diagnostic criteria of tobacco amblyopia is the finding in the centro caecal area of the field of vision of depressed sensitivity to red and green stimuli This is accompanied by a subjective disturbance of colour discrimination Of the tests available for studying this acquired colour defect, we have found the Farnsworth Munsell Hundred Hue test although time consuming most useful This paper reports the results of an investigation by means of this test into the colour vision of patients suffering from treated and untreated tobacco amblyopia

The *Farnsworth Munsell* Hundred Hue test (*Farnsworth* 1943) originally designed for the binocular screening of youthful subjects for congenital colour blindness consists of a graded series of 85 coloured caps arranged in 4 boxes The patient is required to arrange the coloured caps into a regular colour sequence between fixed end caps He is presented with the coloured caps arranged in a standard random fashion In the tests carried out by us no time limit was set for the completion of each box as many of the patients in addition to having defective visual acuity had difficulty in manipulating the caps The tests were carried out on each eye separately using artificial illumination provided by the Hubble Verivide Cabinet which satisfies British Standard 950 part I (1967) The patient s arrangement of the caps is recorded and from this his error score can be calculated and expressed numerically or graphically (Fig 1)

Colours are perceived and discriminated most accurately between the ages

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cine in relation to Mathematics and Computing gave helpful advice on the statistical evaluation of the results Financial aid for this investigation was provided by the Me cine in relation to Mathematics and Computing gave helpful advice on the statistical dical Research Council and Glaxo Ltd

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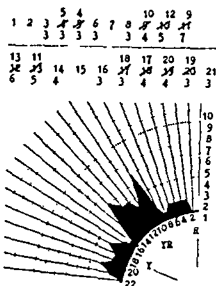


Fig 1
Specimen of Farnsworth Munsell 100 Hue score and profile

of 16 and 35 years (*Lakowski* 1958) After 55 years there is a rapid deterioration in the ability for fine colour discrimination which affects mainly yellow blue or violet blue green discrimination Red green discrimination remains fairly stable and is least affected by age *Verriest* (1963) demonstrated that in normal healthy subjects the error score for the Farnsworth Munsell Hundred Hue test *increased in a positive manner with age from the age of 35 onwards* At the age of 60 years he quotes a mean error score of 95 with an upper limit of 152 for men

Untreated Tobacco Amblyopia

A group of 65 patients of mean age 67 years was composed of 64 males and one female of whom 57 smoked pipe tobacco only 3 cigarettes only and 5 both The mean tobacco consumption of the group was 3 04 ± 1 44 ozs per week They were diagnosed as suffering from tobacco amblyopia after the criteria of *Heaton et al* (1958) The mean error score for the right eye of all patients for the Farnsworth Munsell Hundred Hue test was 732 ±236 In an earlier communication (*Chisholm* 1969) it was suggested that in the case of error scores above 600 a mean of several test results be taken and below 600 a single test result would be sufficiently reliable Where possible this premise was adhered to A typical 100 Hue profile in untreated tobacco amblyopia shows depressed dis

pia The Farnsworth Munsell Hundred Hue profiles obtained in our series of cases show a depression of colour discrimination in most regions of the spectrum but with a predominant red/green loss We have noticed also that with treatment the profile improves slowest in the red green area

The mode of action of hydroxocobalamin in the treatment of this disease is as yet obscure The degree of visual improvement with therapy suggests that the neuro retinal cells have been malfunctioning and on the removal or counter action of the toxic agent have undergone recovery The pallor of the optic disc present initially did not alter on therapy

The Farnsworth Munsell 100 Hue results are a sensitive index of visual function recovery and allow this to be followed quantitatively The Farnsworth Munsell 100 Hue profiles do not establish whether tobacco amblyopia is a disease primarily of the optic nerve pathway or of the neuro retina as discussed by *Schanz* (1920) and *Phillips et al* (1968) The profiles obtained differ markedly from those obtained from Leber s Hereditary Optic Atrophy patients in whom the central visual acuity is also poor but the dyschromatopsia is characteristically of a red green loss

Summary

A defect of colour discrimination is a consistent feature of tobacco amblyopia In the untreated condition the defect takes the form of an irregular depression of colour discrimination in most regions of the spectrum Poor colour discrimination was found to be related directly to poor visual acuity and increased age Sixty patients were treated with parenteral hydroxocobalamin and continued smoking Five patients stopped smoking as their only form of therapy When the disease was associated with pernicious anaemia the rate of visual improvement was slower than that when diabetes was the associated condition When there was no associated disease the rate of visual improvement with hydroxocobalamin was as good as that obtained when smoking was stopped

Acknowledgement

We wish to record our thanks to the various Consulting Ophthalmologistsis of the Western Region (Scotland) who referred cases of tobacco amblyopia We also thank Professor W S Foulds for the use of the facilities of the Tennent Institute Mr G Donald of the Medical Illustration Department Western Infirmary for the illustrations and Mrs M Revans for secretarial assistance Doctor J F Adams Southern General Hospital carried out the vitamin B12 assays Professor W I Card Professor of Medi

crimination in most regions of the spectrum (anarchic profile) with preferential loss in the red/green region

The response of these patients to the pseudo isochromatic plates of the Ishihara pattern (1959) was also examined The results obtained were not as informative as those obtained by the Farnsworth Munsell Hundred Hue test All patients showed a gross abnormality of colour vision some patients being unable to identify the numeral on the first plate which is recognised by all congenital dichromats

The best visual acuity (Snellen) of the right eye of all patients prior to treatment was converted to percentage visual acuity (*Ridley* 1959) The mean visual acuity was found to be 18 % (equivalent to 6/36 Snellen) with a range 1.5 %–100 % The near visual acuity was estimated using the notation laid down by the Faculty of Ophthalmologists (*Law* 1951–52) and similarly transposed to the percentage visual acuity scale The near acuities lay within the range 8 % to 64 % with a mean at 20 75 % (< N18 at 15 inches) No significant difference could be demonstrated between the mean distance acuity and near acuity ($t = 0$ 57 $n = 116$ $p > 0$ 1)

When the Farnsworth Munsell Hundred Hue error score was compared with the distance percentage visual acuity a significant positive correlation was obtained ($= +0$ 402 $n = 62$ $p < 0$ 001) A correlation was also obtained when the Farnsworth Munsell Hundred Hue error score was compared with the patient age ($r = +0$ 325 $n = 62$ $p < 0$ 01) (Fig 2)

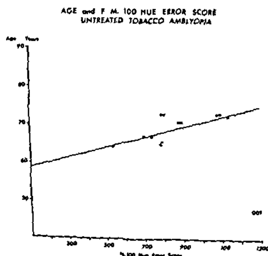


Fig 2
Correlation of Age and Farnsworth Munsell 100 Hue showing regression line in untreated tobacco amblyopia

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Thygeson (1956) found 10 per cent to recover spontaneously while *Laibson* (1964) saw 24 5 per cent to be cured after placebo treatment alone *Burns* found placebo and IDU to be equally effective in the treatment of chronic keratitis or relapses *Davidson* obtained healing of dendritic keratitis in half of his patients within 14 days of instillation of 1 per cent gamma globulin which he himself regarded as a placebo

The immediate success of a treatment (fading of the dendritic pattern and shadowy transformation on IDU treatment and decreasing ciliary congention on steroid treatment) need not indicate a favourable response at the long view

To study the effect of the treatment given I have followed up just over 100 patients to compare the therapy with two of the parametres on which an eva luation of the therapeutic effect on the long view may be based namely the recurrence rate and the visual acuity at the time of the follow up

Present Investigations

The investigation comprised all the patients referred within a seven year period (*1958 1964*) to the Department of Ophthalmology *Kommunehospitalet* with dendritic keratitis i e a corneal affection presenting a typical dendritic pattern

This characteristic disease was described as early as 1884 by the first profes sor ophthalmologiae in Denmark *Edmund Hansen Grut* (keratite ramifiee)

No virus cultivation was performed to verify the herpetic affection the morphological picture being generally regarded as sufficiently specific to justify a diagnosis of herpetic *keratitis*

Incidence

Within the seven year period 157 patients were seen who had had one or more attacks of dendritic keratitis i e 22 4 patients annually

Several of these patients experienced renewed attacks within the seven year period Thus a total of 287 attacks were recorded of which some repeated i e 41 attacks annually

During the same period 6062 patients were admitted to the Ophthalmic Unit while 50270 were treated as out patients Among these a total of 952 had kera titis of some kind or other The recorded cases of dendritic keratitis constituted 1 196 of the total number with ophthalmic diseases

Jonkers found herpetic keratitis to constitute 1 250 of all cases of ophthalmic diseases in Holland

The Department of Ophthalmology *Kommunehospitalet* serves a population of about 700 000 Only a certain proportion of herpetic keratitis cases are referred to the Ophthalmic Out Patient Department a fairly large number being treated ambulatorily by ophthalmic medical practitioners The incidence is accordingly much higher than that recorded in the present paper (59/1 million annually)

In the author s own practice within the same region on an average 10 cases have been recorded each year This corresponds to about 500/1 million annually

The series under review from an ophthalmic unit must be supposed to comprise in particular fairly severe cases while milder cases often have been treated by ophthalmic medical practitioners

Sex and Age

Males predominated definitely in this series 93 males against 64 females (59 per cent males) Male preponderance has been encountered in all the series described It is often even more pronounced than in the present (*Gundersen* 149 males against 75 females *Thygeson* (1956) 135 males against 65 females *Laibson* 72/28 *Jonkers* 154/37 *Sood* 97/53 *Gilles* 100/59)

The age incidence at first attack is shown in table I A fairly large proportion of the cases are grouped within the first ten year period with an equal representation of the two sexes Another maximum within the age group of 40 50 years was due to preponderance of males Males predominated in all age classes above 30

The age distribution shows that the primary infection or an early relapse of

Table I
Dendritic keratitis age and sex incidence 157 cases

age	0	10	20	30	40	50	60	70	80
females	12	9	12	2	11	9	5	4	0
males	12	6	7	14	16	12	13	11	2
Total	24	15	19	16	27	21	18	15	2

24 Ross G I M (1952) Vitamin B12 Assay in Body Fluids Using Euglena Gracilis J Clin Path 5 250
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The equatorial region of both the anterior and posterior parts of the sclera revealed three types of small areas They could produce higher or lower echo amplitudes than the control values or they could divert the sound beam to such extent as made it impossible to register the sound with the described movements of the ball

The lens caused strong attenuation in the axially moving sound while the edges of the lens had much less effect in this respect The edges could however cause a distinct change in the position of the sound beam and they could produce maxima and minima in the echo amplitude curves Those two points of the optic nerve which were examined could either weaken or intensify the sound beam Their echo amplitude curves showed maxima and minima

The results of the experiments show that, depending on the relation between the sound beam and the tissue several kinds of changes may be observed These include attenuation intensification reflection and refraction Under certain conditions total reflection may be observed The intensification of the sound field which is fairly small may be due to the focusing effect of the tissue or to an interference phenomenon caused by it Examinations of the sound fields show that tissues may change the acoustic properties of various parts of any cross sections of the sound field so that they become quite different

Summary

Pig eyes were used for an experimental investigation of the effect of the cornea sclera lens and optic nerve on the sound fields in the various relative positions of the sound beam and the tissues Three different cross sections of the sound field were studied When the sound travelled at right angles through the tissue either strong (the lens) or slight (the cornea and sclera) attenuation was observed When the angle was increased to 30° also the amount of attenuation increased When the sound hit the tissue at a 70° angle it was either reflected attenuated or even intensified The latter phenomenon is probably caused by a focusing effect of the tissue Various tissues may make any cross sections of the sound field very irregular in strength and shape

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From the Ophthalmic Department of the University Hospital
Turku Finland
(Head Professor Arvo Oksala)

EXPERIMENTAL INVESTIGATIONS OF THE EFFECT OF VARIOUS PARTS OF THE EYE ON THE SOUND FIELD IN THE ULTRASONIC METHOD

BY

ARVO OKSALA

Earlier experimental investigations in which one cross section of the ultrasonic field was studied showed that different parts of the eye may considerably change the sound field If the sound travels perpendicularly through the cornea and sclera it will become slightly attenuated (*Oksala & Hakkinen* 1968) When the sound passes the lens axially strong attenuation is observed (*Oksala & Blok* 1968)

If the sound meets the cornea and sclera at an approx 30° angle its attenuation is clearly observed When the angle is approx 70° even a total reflection may be found (*Oksala & Hakkinen* 1969) If the sound passes the edges of the lens slantingly it will be both attenuated and refracted (*Oksala & Blok* 1968) If the sound beam hits the rear eye wall at a 70° angle its course may change because of refraction and possibly because of reflection too The optic nerve may produce an absolute or relative acoustic shadow (*Oksala & Niiranen* 1970)

This study tries in another way to clarify experimentally the effects of the

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mic tonometry also offers accurate registration of the pulse synchronous changes in eye tension i e the corneal indentation pulse Normally the corneal indentation pulse amplitudes average a plunger movement of about 30 microns i e 0 6 scale reading Schiotz A repeated amplitude difference between the two eyes of 15% or more is considered a definite pathological finding (*Horven* 1970)

Clinically the method was applied to the following cases

Case 1 girl aged 14 Extensive cutaneous hemangiomas of face upper part of truncus and extremities as shown in Fig 1 Treated for epileptic attacks from the age of seven months Right sided homonymous hemianopsia with macular sparing left sided F E C changes and calcifications in the occipital cortex as revealed by X ray examination Psychological tests indicates a decreased capacity of learning A rise in intraocular pressure was noted on the left side at the age of 14 years when the first dynamic tonometry examination was performed as listed in Table I She was treated with pilocarpine 4 times daily in left eye At this time eye examination revealed distended episcleral vessels on both sides Corneal diameters were within normal limits and the anterior chambers appeared normal with normal angles as judged by gonioscopy The optic discs showed central physiological excavations and the fundi appeared normal



Fig 1
Case 1

above mentioned parts of the eye on the ultrasonic field The investigation is based on the results of 3 cross sections of the same sound field

Equipment material and method of research

The model of the ultrasonic equipment was Kretztechnik 7000 and the measurements were registered with a Tektronix oscilloscope The 7 5 Mc/2 mm transducer was unfocused The amplification of the equipment was kept at the same level throughout the investigation

For the measurement of the sound field a device was constructed where an SKF steel ball could be moved in three different directions beneath the transducer which had been fixed to a stand The diameter of the steel ball was 1 5 mm and the ball itself worked as a reflector of sound The position of the ball in respect to the transducer could be determined with an accuracy of 0 1 mm The three cross sections of the sound field were obtained by moving the ball first through the sound field via the center of the transducer and then parallel to the first cross section on each side at a distance of 2 mm The amplitudes of the echoes reflected by the ball could be drawn into echo amplitude curves These amplitudes are propotional to the sound pressure at the corresponding points

The material consisted of pig eyes Different calottes were prepared calottes formed by the cornea and the anterior part of the sclera calottes of the posterior part of the eye with and without the optic nerve and lenses with capsules After the transducer and the ball had been immersed in water the above mentioned parts of the eye were placed one after another on a copper wire rack between the transducer and the ball so that the copper wire lay outside the sound field The distance between the transducer and the ball was 30 mm and from the transducer to the nearest point of the tissue 5 mm Control fields were measured in water without the tissues

When the effect of the cornea on the sound field was investigated the sound was first directed perpendicularly to the center of the cornea and then towards its edge With the sclera under examination the sound was first directed to the vicinity of the limbus and then near the equator of the eye When the effect of the scleral rear wall calotte on the sound field was examined the sound first travelled perpendicularly via the center of the calotte and afterwards through its edges While the lens was in the sound field the sound first passed axially through the lens and then through its edges The investigation of the optic nerve was first done at the papilla and then 3–4 mm further back In the latter case an opening was made on the scleral calotte so that the sound hit only the optic nerve Each phase was carried out with 20 different samples of the particular

From Oslo University Eye Department
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CORNEAL INDENTATION PULSE IN STURGE WEBER SYNDROME

BY

T FLAGE & I HORVEN

Sturge Weber syndrome is characterized by nevus of the skin angiomatous involvement of the meninges and brain epilepsy and often glaucoma (*Walsh & Hoyt* 1969)

Congenital glaucoma with bupthalmus is characteristic but glaucoma with later occurence without buphthalmus is also seen Histologic examination has shown angioma of the choroid to be present in a considerable proportion of eyes enucleated for glaucoma (*Dunphy* 1935) Most of the angiomas are flat lesions involving the entire choroid Clinically the angiomas may constitute a choroidal tumor but in most cases the angioma is not visible by ordinary ophthalmoscopy

It is known that the blood volume of the choroidal system is about 37 times that of the retinal system (*Chao P & Bettman J* 1957) Accordingly hemangiomas of the choroid should be of major importance for the pulse synchronous changes in intraocular pressure by yielding an increase in the pulsatile part of the choroidal vascular bed with a corresponding increase in the corneal indentation pulse amplitudes

Material and Methods

Dynamic tonometry is performed by use of an improved electronic tonometer as described by *Horven* (1968) In addition to record the eye tension per se dyna

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part of the eye All investigations were made in a temperature of + 20 C All measurements took place in the far field of the transducer

Results

1 Cornea

When the sound travelled perpendicularly through the center of the cornea all three cross sections of the sound field were very similar to the control measurements made in water The highest amplitude was however in most cases about 1 db lower than in water control When the sound traversed the edges of the cornea 16 cases showed cross section curves which were 2–3 db lower than the control curves but in 4 cases they were 2–3 db higher than the control curves The edges of the cornea usually caused a narrowing in the sound field and 2 maxima and one minimum could often be observed in the curves Fig 1 represents the result of such a measurement The three cross sections of the sound field measured in water control can be seen at the bottom on the left In the middle one can see three cross sections obtained from the sound field when the sound travelled at right angles through the center of the cornea and top right we have the curves from the edges of the cornea They are higher than the control curves and show two maxima and one minimum

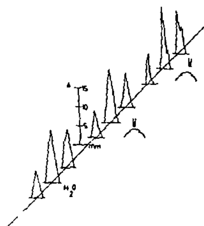


Fig 1
Three cross sections curves obtained through the edges of the cornea (top right) are higher than the other curves

sided buphthalmus with a corneal diameter of 13 mm The disc was cupped but otherwise the fundus appeared normal The left eye revealed normal findings and so did E.E G and X ray examination of the skull

The glaucoma in the right eye could not be controlled medically an iridencleisis procedure was therefore performed on October 7th 1969 Dynamic tonometry results obtained before and after the surgical procedure i e at increased and normal intraocular pressure levels are presented in Table I Fig 3 gives the preoperative dynamic tonometry results which demonstrate a striking increase in corneal indentation pulse amplitudes of right eye

Discussion

The corneal indentation pulse reflects primarily a pulse synchronous change in intraocular pressure initiated by the excess of blood which enters the eye in systole If the pulsatile vascular bed of the eye increases the corneal indentation pulse amplitudes will yield a corresponding increase as may be demonstrated in eyes harboring malignant melanomas (*Horven* 1969)

An increase of corneal indentation pulse amplitudes is also seen in carotid cavernous fistula (*Boyes & Ralph* 1954) during pain attacks of cluster headache (*Broch et al* 1970) and in glaucomatous or experimentally induced ocular hypertension (*Horven* 1970)

In the two cases of Sturge Weber syndrome presented above dynamic tonometry was performed before and after treatment i e at hypertensive and normotensive levels of intraocular pressure At both occations a marked increase in corneal indentation pulse amplitudes was found in the affected eyes As this in

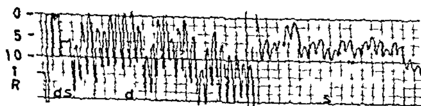


Fig 3

Dynamic tonometry from Case 2 preoperative recording The first part of the curve demonstrates the high intraocular pressure in the right eye The second part demonstrates the increase of the corneal indentation pulse amplitudes of the right eye (d = *right eye* s = *left eye*)

2 The anterior part of the sclera

The sound travelled through the sclera first near the limbus and then near the equator In the former case all cross section curves showed a lowering by 5–10 db in comparison with the control curves In the latter situation one could if one wanted to find near the equator scleral areas which caused in the highest amplitude either a strong fall or a rise (5–10 db) or a reflection of the sound beam to such extent that it could not be found with the above mentioned move ments of the ball These three spots of the sclera were all situated near one another At the same time some maxima and minima appeared and in many cases a transition of the sound beam The latter phenomenon was due to re flection

Fig 2 shows the distinct lowering in the amplitudes caused by the equatorial area of the sclera and the minima and maxima as well as the transition of the beam In Fig 3 one can see a narrowing in the sound beam caused by a corres ponding area of the sclera the maxima and minima and in this case a strong rise in the amplitudes of all three cross sections

3 The posterior part of the sclera

When the sound passed the center of the calotte at right angles the cross sec tion curves were very much like the control curves but mostly 1–2 db lower than them The edges of the calotte on the other hand revealed spots which produced either a distinct rise or a fall (approx 5–10 db) in the highest ampli

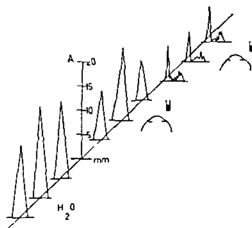


Fig 2

Three cross sections curves obtained through the equatorial area of the sclera (top right) are distinctly lower and more irregular than the other curves

Table I

Intraocular pressure and corneal indentation pulse amplitudes (μ) in two cases of Sturge Weber syndrome

Case No	Date	Treatment	Intraocular pressure in mm Hg (P_0) right	left	Corneal indentation pulse amplitudes right	left	% ($\frac{P\ 100}{N}$)
1	Dec 13 1967	Before	20 6	34 5	45	90	200
	Jan 31 1968	After	18 9	12 2	52	88	169
2	Oct 2 1969	Before	41 4	13 4	60	16	375
	Nov 3 1969	After	18 9	15 9	16	10	160

by ophthalmoscopy Under pilocarpine treatment which controlled the glaucoma on the left eye a second dynamic tonometry examination was performed as *shown in Fig 2 The first dynamic tonometry examination performed when the* intraocular pressure was pathologically increased on the left side demonstrated a marked difference in corneal indentation pulse amplitudes of the two eyes reading 45 microns on the right eye an 90 microns on the left (Table I) This difference was still present at the second dynamic tonometry examination which was performed at a normal intraocular pressure on the left side which proves that the increased amplitudes on the left eye are not primarily caused by a difference in eye tension levels on the two sides

Case 2 boy aged 7 Cutaneous hemangiomas in upper right side of face in the region supplied by *the first and second division of the trigeminal nerve He* is lefthanded and had some *difficulties in learning to pronounce words Right*

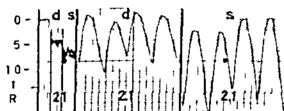


Fig 2

Dynamic tonometry from Case 1 after control of her glaucoma The first part of the curve demonstrates a lower intraocular pressure in the left eye The second part demonstrates the increased corneal indentation pulse amplitudes of the left eye (d = right eye s = left eye)

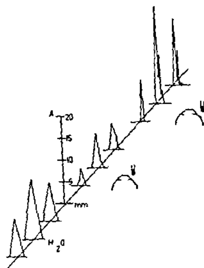


Fig 3

Cross sections obtained under similar conditions as the ones in Fig 2 In this case when the sound has traversed the sclera near the equator the curves are however higher and narrower than at the control examination.

tude when compared with the control curve as well as some maxima and minima If so wanted one could at this examination too find near the edge of the calotte a small area which deverted the direction of the sound so much that it could not be found with the described movements of the ball Fig 4 represents the results of an examination in which the three cross section curves at the top on the right are distinctly lower than the rest of the curves

4 The lens

When the sound travelled axially through the lens the curves were approx 25-30 db lower than the control curves When the examination was made through the edges of the lens the echo amplitudes that were registered were lower than in the control test but higher than at the axial examination Fig 5 shows the results in one lens When the sound traversed the lens axially the curves were very low while the edges produced distinctly higher echo amplitudes than the axial examination. The edges of the lens may cause the appearance of clear maxima and minima as well as a transition in the position of the beam due to the refraction

(From the Eye Clinic Head R Tornquist M D Regional Hospital Orebro Sweden)

TREATMENT OF THE POSTOPERATIVE HYPOTONY SYNDROME

(Preliminary Report)

BY

RAGNAR TÖRNQUIST

The hypotony associated with shallow anterior chamber and choroidal detachment which may follow operations for cataract or glaucoma is usually caused by an external fistula (Meller) Even if this complication develops some time (weeks or months) after the operation the explanation is the same The rational therapy is to close the fistula and this is usually successful Great emphasis is laid on the importance of the fluorescein test (Seidel s sign) for localisation of the fistula

According to Hagen if the fluorescein test is negative there may still be a microfistula Such cases may be more difficult to treat but in one case which followed Stallard s iridencleisis Rosengren obtained an immediate effect by the application of a silicone plomb over the site of the operation

At the Eye Clinic in Orebro the same therapy has been used successfully in the cases of two patients

Case Reports

1 4 u *na t born 1897* who since 1964 had been treated for glaucoma simplex of both eyes In 1965 a thrombosis of the central retinal vein developed in the *left* eye It was followed by clouding of the lens and marked reduction of vision On 9th September

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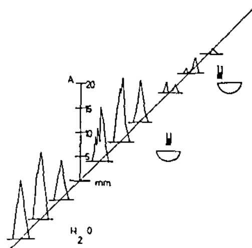


Fig 4

Cross sections curves when the sound passes through the posterior calotte of the sclera Examination revealed a point near the equator which considerably lowered the echo amplitudes in comparison with the control values

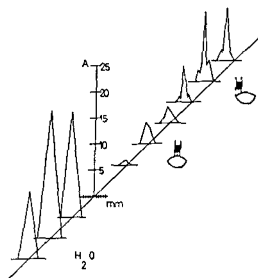


Fig 5

Cross sections of the sound field with the sound passing first axially through the lens and then through its edges Axial attenuation is quite strong

5 The optic nerve

The examination was made at two different points the sound either passed the center of the calotte and pierced the papilla or it travelled through the opening

crease was present also at normal levels of intraocular pressure it may not be fully explained by the initial ocular hypertension It is therefore presumed that the increase in corneal indentation pulse amplitudes observed in these cases should mainly be explained by an increase of the choroidal pulsatile vascular bed The existence of choroidal angiomas in these cases are most likely even if such were not seen by ordinary ophthalmoscopy

Summary

Dynamic tonometry is presented as an easy way to prove ocular angiomatous involvement in patients with Sturge Weber syndrome

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made on the sclera and hit the optic nerve 3–4 mm further back In the former position the curves became 10–15 db lower than the control curves in 6 measurements out of a total of 20 in one measurement they were 2 db higher and in 13 measurements they were almost the same as the control values In the latter position the curves were *in 3 cases approx 10 db lower and in 17 cases 2–5 db* higher than the control curves All curves showed maxima and minima Fig 6 shows how the area of the papilla causes a distinct fall in the intensity of the sound field while the part of the optic nerve which is further back intensifies the sound field

Comments

If the sound passes perdendicularly through the calotte of the cornea and sclera the cross section curves of the sound fields show only slight changes when compared with the control curves They may become somewhat lower and narrower When the sound travels through the cornea and sclera at an approx 30 angle there is usually a greater fall in the curves with some maxima and minima While cornea alone was the object of study the curves were found to be higher than the control values in four cases

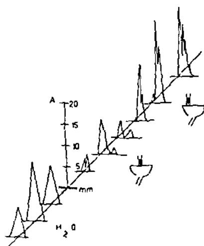


Fig 6

Cross sections when the sound passes through the optic nerve first at the papilla and then 3–4 mm further back In the former case considerable attenuation was observed In the latter case the echo amplitudes are higher than at the control examination

Discussion

The postoperative hypotony syndrome has a tendency to resolve spontaneously after varying intervals Assessment of the efficacy of various therapeutic measures is therefore difficult Many methods of treatment have been described (mydriatics miotics carbonic anhydrase inhibitors pressure bandaging etc) Good results have been ascribed to most of these measures The value of the method described here is uncertain because of the only limited experiences That the immediate effect have persisted for a considerable time in all cases implies that the procedure has been therapeutically effective

Further studies of the effects of this method under different conditions as well as experimental work should make it possible to identify the pathogenesis of the postoperative hypotony syndrome In particular the theories concerning the origins of the choroidal detachments are uncertain and merit further study

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Oksala A & Hakl inen L Der Einfluss der Augenhulle auf das Schallfeld Experimen

1968 a *cyclodialysis* was performed on the *right* eye The postoperative course was complicated by hyphaema with markedly raised intraocular pressure On 19th September irrigation of the anterior chamber was carried out and at the same time an *Elliott's trephination* was performed The intraocular pressure was reduced to normal but because of increasing lens opacification it was necessary to perform an *intracapsular lens extraction* on 14th May 1969 *(with alpha chymotrypsin) The postoperative course* was free from complications The visual acuity was 1 0 with correction on 20th November *1969*

On 16th January 1970 there developed spontaneously a painful and rapid deterioration of the vision of the right eye On examination three days later the vision was reduced to counting fingers at three metres The anterior chamber was very shallow The subconjunctival fistulation following the trephine operation seemed to be functioning well but no external *fistula through the conjunctiva was seen* Large choroidal detachments were seen at the periphery of the fundus and the intraocular *pressure was very low*

On 26th January a silicone plomb (silastic) was applied on the conjuctiva over the trephine opening in the sclera Pressure was achieved by stretching the plomb before the episcleral sutures were tied Four to five hours later the intraocular pressure had risen to 42 mmHg and therefore the tension of the plomb was slightly reduced Two days later the anterior chamber was still very shallow and the intraocular pressure was 24 mmHg The silicone plomb loosened spontaneously and was therefore removed on 29th January On 3rd February *the anterior chamber* appeared to be of normal depth and about one week later the choroidal detachments had completely disappeared *On examination on 15th April the visual acuity was 0 7 with correction* The intaocular pressure was 14 mm Hg The anterior chamber was reformed and there was no choroidal detachment

2 *A woman born 1906* At a routine refraction on 4th March 1970 raised intraocular pressure in both eyes was found The anterior chamber of each eye was rather shallow Gonioscopy revealed a narrow chamber angle in each eye (0–1 degree) Tonography showed C of the right eye to be 0 13 and C of the left eye to be 0 15 The intraocular pressure was not satisfactorily controlled with medical therapy and on *10th March 1970* a *sclerectomy* was performed on the *right* eye Postoperatively a *widespread choroidal* detachment developed *and the anterior chamber* became more shallow As the pressure in the *left* eye was not satisfactorily controlled with medical therapy a *sclerectomy was performed on this eye on 24th March 1970 In this* eye also a large choroidal detachment developed and the anterior chamber became completely lost There was marked hypotony of both eyes No fistula through the conjunctiva could be demonstrated As the condition appeared to be stationary on *9th April 1970* an *anterior sclerotomy and injection of air into the anterior chamber* was performed on the *left* eye and on *16th April 1970* the same operation was performed on the *right* eye Only a transient improvement was obtained and several days later the condition was unchanged On *28th April 1970* a *silicone plomb* was applied to the *left* eye over the conjunctiva *covering the scleral fistula* The anterior chamber *reformed* at the time of the operation and the choroidal detachment disappeared after a few days On 5th May the plomb was removed The same operation was performed *on the right eye* on *5th May 1970* and the anterior chamber deepened somewhat but the choroidal detachment did not disappear The plomb appeared to be in corectly placed and *therefore* a further operation was performed on *11th May 1970* and a larger soft silicone plomb was applied over a greater area The anterior chamber returned ofter a few days *and the choroidal detachments disappeared* completely

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Oksala A & Hukkinen L Experimental studies of the behavior of ultrasound in the sclera and cornea In Ophthalmic Ultrasound ed by Gitter Keeney Sarin and Meyer Mosby Saint Louis 1969 pp 59–64
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ces occurred in only one patient One year previously this patient had sustained severe cranial injury Four hours after the encephalography transient blindness occurred The X rays showed bilateral cortical atrophy Nothing is stated about the aqueduct or the 4th ventricle

In 1954 *Reese* (*1*) reported a series of 16 patients with bilateral homonymous hemianopsia in 3 of whom the blindness had arisen in connection with ventriculography The diagnoses had been hypertension with severe headache craniopharyngioma and increased intracranial pressure of unknown aetiology *Reese* was the first to point out the possible pathogenetic role of the posterior cerebral arteries Incarceration of these vessels in the tentorial notch owing to a difference in pressure above and below the *tentorium cerebelli* or possible spasms in the vessels might explain the blindness as being of cortical nature In further support of this theory *Reese* reported a case of bilateral homonymous hemianopsia in which autopsy showed the cause to be thrombosis in the basilar artery extending into both posterior cerebral arteries associated with bilateral cortical necrosis of the occipital lobes This not uncommon post mortem finding had previously been described by *Moore & Stern* (6) (1938)

Rinaldi et al (8) (1961) described 5 patients who developed cortical visual disturbances after ventriculography and/or ventricular decompression

In 3 patients with pinealoma or tumour of the 3rd ventricle a Torkildsen drain was inserted after the ventriculography All developed lasting blindness with preserved pupillary reaction and two also Anton s syndrome Two of the patients who died 2 months and 1 year later came to autopsy and in both cases the visual cortex was found to be normal grossly as well as microscopically One patient had a tumour in the 4th ventricle but in this case (a girl aged 4 years) the blindness was transient Three days after the operation perception of light had returned and another 17 days later vision was restored

In these 4 patients the visual loss may have been due to incarceration

The 5th patient had metastases from a malignant melanoma with symptoms of massive incarceration In this case autopsy revealed cortical infarction in both occipital lobes

Rinaldi s 5 patients differ from those mentioned above and from ours in having had operation in connection with the ventriculography Therefore the ventriculography cannot be interpreted as the sole aetiological factor in the blindness

Lossius (4) (1955) reported 3 cases of impaired visual acuity and homonymous quadrantic anopsia in the left lower quadrant following ventriculography In all 3 cases the visual field defects subsided spontaneously

Present Investigations

The author perused the records for 335 patients who had ventriculography in

ten was locali ed in the cornea while attacks of keratitis occurring later in adults may have been provoked by injuries at the place of work a fact which possibly accounts for the male preponderance

However only few patients gave a history of injury immediately before the eruption of herpes on the cornea

The age and sex incidence noticed corresponded fairly closely to that in *Gundersen's* series in which the age classes under 16 comprised 23 males and 23 females while of the patients above this age 126 were males and 52 females

Gilkes likewise found maximum of cases within the age group of 40 50 years while only few patients were under 10 *Sood* noticed preponderence of females in the age group under 10 years and preponderance of males in the group over 30 In *Laibson's* series the majority were in the forties

Seasons

Herpetic keratitis is often released by a cold influenza or the like The attacks might be conceived to occur particularly often within certain *seasons* The month of onset of each attack (both first attack and relapses) is recorded in table II in as far as the time of onset is known

The attacks are seen to have been fairly equally distributed over the whole year with no particular accumulation within the months where colds prevail On the contrary the number was somewhat greater during the six summer months (136) than during the six winter months (90)

This result – no significant seasonal variations – contrasts with those of other workers Thus *Gunderson* found the greatest number of cases in September and October *Jones* in September *Brandt et al* in spring *Laibson* in January February and March and *Schenk & Hummer* (quoted by *Jonkers*) a similar predominance

Jonkers observed no seasonal variations

Table II

Numbers of herpetic ke atitis attacks within the individual months 226 recorded attacks on an average 19 attacks per month

month	1		3	4	5	6	7	8	9	10	11	12
number of attacks	18	14	17	24	4	14	22	25	27	13	14	14

We may thus probably be justified in concluding that no seasonal variations exist

Follow-up

The follow up was in all cases carried out by the author himself Of the total series of 157 patients 109 were followed up 27 had died at this time Of these 21 would have been over 70 four in the 60ies and two in the 50ies at the time of the follow up if alive

The remaining 21 (13 per cent of the total series) were not followed up because the adress was unknown (3) the patient was away (6) admitted to another hospital (2) placed in a remand home (1) or failed to appear for examination (9)

The 109 patients followed up are described below

Bilateral Cases

Herpetic keratitis is usually a unilateral affection and relapses occur in the same eye

However in ten of the 109 the affection came on simultaneously in both eyes and in one case there was keratitis in one eye and recurrence in the contralateral eye Most of the patients with bilateral keratitis were children (six were under 10)

Only one patient experienced considerable impairment of vision of both eyes (a man aged 55)

Gunderson found 1 per cent bilateral cases among 221 patients *Laibson* 2 per cent (150 patients) *Sood* likewise 2 per cent (150 patients) *Thygeson* 9 5 per cent (200 patients) The 10 per cent bilateral cases in the present series is thus a high figure compared with those of previous statements

Primary Herpetic Keratitis

Primary keratitis was a likely diagnosis in seven of the 109 cases (follicular conjunctivitis or vesicles on eyelid forehead nose or cheek simultaneously with first attack of herpetic keratitis) Four of these cases were bilateral

Thygeson (1956) found 4 5 per cent primary cases

Herpes of Lips

Recurrent herpes of the lips is often seen in patients with dendritic keratitis

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BILATERAL HOMONYMOUS HEMIANOPSIA FOLLOWING VENTRICULOGRAPHY

BY

K E RASMUSSEN

Bilateral homonymous hemianopsia is taken to mean blindness showing hemianoptic nature in the course of its development or regression In bilateral homonymous hemianopsia there is loss of both halves of the visual field in both eyes in other words the patient is extremely amblyopic or totally blind

This visual disturbance has been reported following ventriculography by several authors

The first report was *Masson s* (5) from 1933 Among 100 consecutive cases of ventriculography he found 6 of temporary blindness Four of these patients had intracranial tumours (3 had choked discs) and two had symptoms suggesting encephalitis

In 3 of the patients with intracranial tumours several hours elapsed from the ventriculography until operation or puncture done to equalize the difference in pressure over the tentorium cerebelli In these cases therefore there could have been incarceration from above with consequent circulatory disturbances in the visual cortex and visual pathways In these cases the visual disturbances did not occur until 2–4 hours after the ventriculography while in the last of the patients with intracranial tumour the blindness developed after evacuation of only 2 ml cerebrospinal fluid before the injection of air (the same occurred in one of the patients with encephalitis) In this case and in the two patients with encephalitis the cause had to be interpreted as injury to the white matter around the collateral trigone

Among 501 lumbar encephalographies Masson found that visual disturban

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Summary

Eight cases of bilateral homonymous hemianopsia were found following ven triculography on a material of 335 patients In 5 of these cases the vision re turned to normal in less than 10 days in one it had been restored at follow up 6 months later while in 2 cases no improvement had occurred at discharge from hospital 1 and 2 months after the ventriculography

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Two hours postoperatively she had no perception of light. Her pupils were dilated of equal size showing sluggish reaction to light Only slight venous congestion no venous pulsation Ophthalmoscopy otherwise unchanged

On the day after the ventriculography the vision was finger counting at 2 m on both sides The right pupil was smaller than the left both reacted to light the left more sluggishly than the right Visual field for fingers Left sided homonymous hemianopsia

On the second day after the ventriculography no visual field defect was de monstrable and 9 days after the visual acuity in both eyes was 1 0 Pupils na tural Visual field for fingers showed no defects Ophthalmoscopy unchanged

Three months later blurred outlines of the discs without measurable promi nence normal visual acuity and perimetry

EEG 3 days prior to the ventriculography had shown a slightly abnormal curve with (4) 5 7 hz activity over both hemispheres without any definite dif ference between the two sides Five hours after the ventriculography EEG showed a moderately abnormal curve with rather sparse alpha activity and quite some (3) 4 7 hz activity over both hemispheres without any difference between the sides and especially posteriorly over the hemispheres Periodical bi occipital dampening Normal occipital blocking on opening the eyes

EEG 10 days after the ventriculography showed moderately severe abnorma lities of the curve with sparse alpha activity over the right hemisphere and right sided preponderance in the temporo occipital regions of low frequent ac tivity of (2½) 3 6 hz On the basis of the EEG findings it could not be decided whether the lesion was in the cortex or in the white matter

Case 2 (G 333/0) Diagnosis Cerebral arteriosclerosis insufficiency of cerebral circulation

A woman aged 57 with arterial hypertension Three years previously she had been admitted to an eye department with bilateral chronic chorioretinitis At that time her blood pressure had been 210/110 Two weeks before her transfer to the neurosurgical department the patient had been admitted to a department of medicine after a subacute cerebral insult. She had right sided hemiplegia and aphasia but mentally she was awake and oriented Blood pres sure 210/110 – 1/0/100

At the ophthalmological examination on admission the visual acuity had not been determined Ophthalmoscopy showed old chorioretinitic changes but nothing else of note Visual field for fingers natural

Left sided carotid arteriography revealed delicate vessels throughout but no definite signs of space filling lesions To rule out a parietal haematoma ven triculography was performed While occipital burr holes were being made un der local anaesthesia the blood pressure fell from 165/90 to 80/50 After injec tion of Pressomin the blood pressure rose to 200 but gradually dropped again

ties as the sole finding in women and children of families with Fabry s disease In *Spaeth & Frost s* review the corneal opacities were described in 47 out of 51 cases

Abnormalities of vessels in conjunctiva

The vascular abnormalities in the conjunctiva consists of small focal varicosities and ampulliform or saccular dilatations and tortuosity of the vessels *Rahman* found these changes in all males (8 patients) but could not demonstrate them in any females (6 patients) *Spaeth & Frost* noted that 26 out of 43 patients in their review showed similar findings *Colombi et al* could not demonstrate conjunctival abnormalities in any of their 10 patients

Abnormalities of the retinal vessels

These abnormalitiesare limited to the veins which may show angulation tortuosity and haustrations In their review of 77 cases including 12 of their own *Spaeth & Frost* noted abnormal retinal vessels in 25 out of 46 cases *Colombi et al* found that 2 out 10 patients belonging to one family had similar retinal lesions

Other ocular abnormalities

In addition to the above mentioned findings periorbital oedema oedema of the fundus optic nerve atrophy and discrete stellate cataracts have occasionally been described in patients with Fabry s disease

Present series

15 members of one family (family I) fig 1 and table I were examined 4 did not show any symptoms or signs of the disease 7 females and 4 males did have the characteristic symptoms from the extremities 3 females and 3 males had other general manifestations of the disease (from kidney heart lung and central nervous system) These findings are described in detail elsewhere (*Christensen Lou* 1970)

The 7 females and 4 males with a history suggesting Fabry s disease all had characteristic skin and/or eye changes (figs 2 3 4 5 and 6) Five women presented skin lesions and in one of these aged 30 years these were the only sign Five out of seven women showed pronounced corneal opacities while corneal changes could not be demonstrated in the other two On the other hand corneal opacities were the sole findings in two women aged 18 and 30 years respectively Faint corneal opacities were seen in two males while this finding was question

the Department of Neurosurgery G Århus Kommunehospital, during the 10 year period 1956–1966 In 172 cases the diagnosis was encephalitis and in 163 cerebral arteriosclerosis

These two diagnostic groups were selected because none of the patients had undergone intracranial operations in connection with the ventriculography Therefore the ventricular puncture may be considered a probable aetiological factor in bilateral homonymous hemianopsia

Among the 335 patients studied, bilateral homonymous hemianopsia developed in only eight cases

Case 1 (G 33224) Diagnosis Chronic encephalitis

A 13-year old girl who had previously been in good health Through the past 2 years she had been suffering from attacks of frontal pressure headache during the first 18 months accompanied by nausea and vomiting For 3 months there had been brief episodes of blurred vision and diplopia especially when she was looking at the blackboard at school transient dizziness, and blackening before the eyes when arising in the morning General condition unaffected

Neurological examination showed no abnormalities Admitted because the ophthalmologist found choked discs

Ophthalmological examination on admission Visual acuity in both eyes 1 0 Pupils and ocular movements natural Ophthalmoscopy Small reddish discs surrounded by greyish tissue mainly on the nasal aspect prominence 1–2 dioptres Veins dilated faint venous pulsation Perimetry 6/2000 for white and 10/2000 for red Slightly enlarged blind spots

To measure the intracranial pressure through 24 hours a drain was inserted into the lateral ventricle Burr holes were made in the usual sites in the occipital region for ventriculography On the right it was difficult to come on the ventricle There was only a slightly elevated pressure and the inserted plastic drain was soon occluded Therefore the drain was removed and re inserted on the left Now the pressure in the ventricle was low and only a couple of ml cerebral fluid were evacuated During the latter part of the procedure the patient was restless and complained of black spots before the eyes A quarter of an hour later she was unable to see Both pupils were dilated the left one inactive to light while the right one gave a very faint direct reaction The patient was agitated slightly delirious The pressure meter showed no excursion Blood pressure 130/70 (as prior to the procedure)

The catheter was removed and ventriculography was done with puncture of both posterior horns The ventricles were small Otherwise the films showed normal appearances No signs of space occupying lesions The patient was believed to have encephalitis and the blindness was interpreted as a result of oedema so that concentrated type specified serum was administered On this treatment the patient became entirely rational but remained blind

The biochemical defect is a lack of a ceramide trihexoside cleaving enzyme (*Brady et al* 1967) leading to widespread accumulation of trihexose ceramide in the vessel walls and in the parenchyma of different organs mainly kidney and heart (*Sweeley & Klionsky* 1963 *Christensen Lou* 1966) Extensive pathological studies have been carried out by *Pompen et al* (1947), *Scriba* (1950) and *Jensen* (1966)

In males the first symptoms occur in childhood as attacks of severe pain peripherally in the limbs The pain is provoked by fever as well as by increased temperature in the surroundings Periods of fever and headache are prominent in many cases Skin and eye manifestations may often be present from childhood The course of the disease is often dominated by continuously deteriorating kidney function leading to death between 30 and 55 years of age Cerebral and cardial symptoms may be present to a varying degree In females the symptoms generally occur at a later age are less prominent and the prognosis is usually good

The first feature of this disease to be noticed was the characteristic skin manifestations In males the cutaneous lesions generally appear about the age of 10–20 years In females the lesions are less frequent and less prominent and tend to occur at a later age The skin lesions are so frequent that *Wise et al* (1962) postulated that every patient with symptoms of Fabry s disease presents these lesions In recent years however it has become apparent that the skin lesions are not always present in Fabry s disease For example they may be lacking in young individuals and in females (*Jensen* 1966 *Colombi et al* 1968) *The skin lesions consist of pin point to hemp seed sized brownish red* often slightly elevated elements which do not become anaemic on pressure (Fig 3) The lesions often have a characteristic distribution being localized on the lower trunk genital region and upper thigh (Fig 2) Such skin manifestations are exclusively found in Fabry s disease (*Borch-Jorgensen & Borch-Jorgensen* 1965) In cases where skin lesions are lacking or doubtful eye manifestations may be present and of great value in the diagnosis

Steiner & Voerner described retinal vascular tortuosity in 1909 and aneurysmal vessels of the conjunctiva and corneal opacities were noted by *Weicksel* in 1925 *Rahman (1963)* and *Spaeth & Frost* (1965) have described these findings very thoroughly

Corneal opacities

The initial changes are described as a slight dust like haziness of the cornea The more advanced changes consist of whitish whorled streaks arranged in a vortex the center of the cornea The lesion is localized to the deep part of the corneal epithelium In *Rahman s and in Colombi et al s* materials all patients presented corneal changes *Colombi et al* (1967) have described corneal opaci

EEG before the ventriculography had shown a slightly abnormal curve (6 8 hz diffusely) Nine days later it showed a slightly to moderately abnormal curve (5 7 hz diffusely 7 hz in the right occipital region))

Histological diagnosis Mild meningitis mild chronic ganglion cell degeneration

Case 4 (C 16208) Diagnosis Meningitis cerebral metastases

A woman aged 20 who had been suffering from fatigue during the past 6 months and in whom a large abdominal tumour had been demonstrated two weeks before admission For the past 2 weeks bilateral peripheral facial palsy headache and vomiting as well as visual disturbances including diplopia.

Ophthalmological examination at admission Mild gaze paralysis of conjugate movement to the right Visual acuity in both eyes 1 0 Ophthalmoscopy and visual field for fingers normal

Ventriculography revealed normal ventricles and pressure (160 180 mm of water) 7 + 10 ml of slightly blood admixed to clear cerebrospinal fluid was tapped

Immediately after the ventriculography the patient complained of being unable to see The vision slowly returned and on the next day it had been fully restored The ventriculography showed normal appearances

The patient died 4 weeks later Autopsy showed acute meningo encephalitis and a metastasis in the right occipital pole immediately supero laterally to the calcarine fissure – from an ovarian carcinoma

Case 5 (G 18624) Diagnosis Encephalitis choked discs

A woman aged 24 who had two weeks before admission developed severe frontal occipital headache with a few vomitings and a temperature up to 38° C as well as some rigidity of the neck Three days later diplopia lasting for a couple of minutes

Ophthalmological examination at admission Visual acuity on both sides 1 0 Ophthalmoscopy Choked disc with a prominence of 1 dioptre on the right and less than 1 dioptre on the left Perimetry 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At ventriculography under local anaesthesia the ventricles were found to be normal and there were no signs of space filling lesions or dilatation. Pressure 40 / 0 mm of water 21 + 2 ml of clear to slightly blood admixed cerebrospinal fluid was evacuated Blood pressure 120/80 constant during the procedure

After the ventriculography she went completely blind but her vision returned the same evening On the next day she complained of blurred vision Two days after the ventriculography ophthalmological examination showed a visual acuity of 1 0 in each eye Ophthalmoscopy was unchanged from prior

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to 140/80 Both ventricles were punctured without any complications and 1 ml fluid was tapped from the right side 3 ml from the left Pressure 100 mm of water Thereafter air was insufflated During the insufflation the patient became remote and later vomited As X rays showed that all the air was on the surface of the brain the ventricles were again punctured but as they now yielded only a few drops of cerebrospinal fluid no more air was insufflated

Now, the patient complained of being unable to see Visual field examination (with fingers) immediately after the ventriculography showed questionable left sided homonymous hemianopsia Eight hours later the patient was able to see hand movements at 1 m on the right and at 75 cm on the left Now there was definite left sided homonymous hemianopsia for fingers and a superior right sided quandrantic anopsia Ophthalmoscopy unchanged On the next day the visual acuity on the right was Hand movements at 1 m On the left Finger counting at 1 m Visual field defect unchanged

Two months later the appearances were unchanged Visual acuity on the right Finger counting at 1 m Left 2 m Visual field defect unchanged Left sided homonymous hemianopsia and right sided superior quadrantic anopsia

Case 3 (G 22075) Diagnosis Suspicion of cryptogenic encephalitis Choked discs

A woman aged 29 who had been having during the past 4 5 months brief episodes of blurred vision and obscurations up to several times daily initially in the left eye and during the past month also in the right Moreover there had been a period of one week with diffuse pressure headache without pressure exacerbations or other associated phenomena Ophthalmological examination showed on admission Visual acuity in both eyes 1 0 Ophthalmoscopy Discs hyperaemic prominence 3 4 dioptres Small haemorrhages on both discs Visual field for fingers normal

At ventriculography under local anaesthesia the pressure was 270 310 mm of water Blood pressure 140/85 constant during the procedure On both sides 11-12 ml first slightly blood admixed later clear cerebrospinal fluid was tapped A cortical biopsy was taken The X rays showed all the air on the surface During the ventriculography the patient complained of malaise and headache and at its completion she was blind (but with preserved perception of light)

On the following day vision began to return (not examined) Ophthalmological examination 3 days after the ventriculography Vision in both eyes less than 1 0 Ophthalmoscopy Unchanged from prior to the ventriculography Visual field for fingers natural

Four days later another ventriculography was performed but again failed This time there were no complaints of visual disturbances and subsequent ophthalmological examination showed unchanged condition

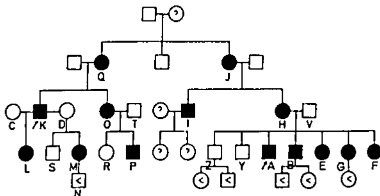


Fig 1

Family I Information is lacking in the first generation of the pedigree Hospital charts indicated the presence of Fabry s disease in the cases J I and Q K O and H and all members of the next generation (except for two living in the U S A) were examined by the authors and Fabry s disease was diagnosed in all cases except S R Z and Y which did not show any symptoms or signs of the disease The last generation consists of small children and infants At presence it is impossible to determine whether they are in volved or not

able in the other two In the last two cases the patients died from the systemic lesions of Fabry s disease and thus could not present for repeated examination

In one woman 25 years of age abnormalities could be demonstrated in the conjunctival vessels and in another woman aged 57 years abnormalities were present in the retinal vessels On the other hand abnormalities of the conjuncti val vessels were seen in all males and of the retinal vessels in all males except one

Comment and conclusion

The most frequent ocular manifestation in patients with symptoms of Fabry s disease is corneal opacities occuring with about equal incidence in males and females Corneal opacities are often more pronounced in females than in males independent of the degree of skin and/or other manifestations of the disease

Although similar corneal changes have been described in cases of chloroquine poisoning and in cornea verticillata a corneal degeneration possibly unrelated to Fabry s disease the corneal opacities are highly characteristic of Fabry s disease and are of special diagnostic value in the heterozygote females and young males

In the present series all men and one woman with symptoms of Fabry s dis ease showed characteristic conjunctival vascular lesions The occurrence of such conjunctival lesions in a woman has not been described previously The finding

tigue and impairment of memory 11 days before admission suddenly severe occipital headache with blurred consciousness and incontinence of urine

On admission he showed rigidity of the neck a blood admixed cerebrospinal fluid mental deterioration but she was awake and fairly oriented as to her own data but not as to time and place

Ophthalmological examination at admission Vision in right eye 0 5 in left eye 0 67 Ophthalmoscopy Arteriosclerotic vessels but no other abnormalities Visual field for fingers normal

EEG revealed a moderately abnormal curve

On ventriculography the pressure was 50 70 mm of water Pronounced diffuse symmetrical atrophy of the ventricles Blood pressure 140/80 constant during the procedure

After the ventriculography the patient was torpid with sluggish reactions Therefore concentrated dry serum was administered and ventricular puncture was performed repeatedly

Gradually the patient awoke but was still severely deteriorated mentally and she gave an impression of being unable to see

20 days after the ventriculography the visual acuity could be determined At that time the vision on the right was perception of light and on the left hand movements in front of the eye Ophthalmoscopy Arteriosclerotic vessels and a small streaked haemorrhage at the right disc No other abnormalities

One month after the ventriculography the haemorrhage had disappeared Otherwise the ophthalmological findings were unchanged The visual field could not be determined

A cortical biopsy showed chronic meningo encephalitis

The patient was transferred to a nursing institution

Case 8 (G 16075) Diagnosis Suspicion of encephalitis

A woman aged 31 who had been suffering through 3 years from right sided frontal temporal headache orthostatic episodes on sudden changes in the position of the head and blackening before the eyes During the past 6 months decreasing visual acuity in the left eye

Ophthalmological examination showed visual acuity on the right to be 1 0 and on the left 0 5 Ophthalmoscopy Choked discs with a prominence of 2 dioptres Perimetry 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At ventriculography 6 + 1 ml of a blood admixed cerebrospinal fluid was tapped Pressure 260/340 mm of water The X rays showed no signs of dilatation of the ventricular system or of space occuping lesions.

After the ventriculography the patient complained of blurred and impaired vision in both eyes but finger counting was possible at 20 cm

Code (conf fig 1)	Fe[illegible]						Males				
	IL	IL	II	IM	IG	IO	III	II	IB	IA (died)	IK (died)
Age at latest examination (years)	18	25	29	30	31	49	57	17	30	32	54
Visible skin lesion	−	+	+	−	+	+	+	+	+	+	+
Vessel abnorm in fundus	−	−	−	−	−	−	+	+	+	+	−
Vessel abnorm in conj	−	+	−	−	−	−	−	+	+	+	+
Corneal opacities	+	+	−	+	−	+	+	+	+	?	?
Eye findings	+	+	−	+	−	+	+	+	+	+	+
Proteinuria	−	−	−	−	−	−	+	−	−	+	+
Azotaemia	−	−	−	−	−	−	−	−	−	+	+
Hypertension	−	−	−	−	−	−	−	−	−	−	−
EKG abnormalities		−					+			−	+
Cardiomegaly		−	−				+		−	−	+
Spontaneous pneumothorax	−	+	+	−	−	−	+	−	−	−	−
Febrile episodes	+	+	−	+	−	−	+	+	+	+	+
Fever and Heat provoked	+	+	+	+	+	+	+	+	+	+	+
Pains in extremities											
Periodical headache	+	+	+	+		−	−	+	−	+	+
Neurological deficits		−	−	−	−	−	+	+	−	+	+

+ Verified anamnestically and/or objectively − Disproved

A completely negative clinical examination and history was obtained in the cases S R Y and Z at the ages of 18 22 38 and 44 respectively (Fig 1)

to the ventriculography Visual field for fingers Left sided homonymous hemianopsia

Five days after the ventriculography there was left sided inferior quadrantic anopsia and 16 days later normal perimetry

At the ventriculography a piece of the cortex was removed for microscopic examination which showed normal appearances

Case 6 (G 24051) Diagnosis Encephalitis

A boy, aged 14 years with a familial predisposition to angioreticuloblastoma Admitted after some attacks in which he fell without losing consciousness or having convulsions

Ophthalmological examination at admission Visual acuity on the right 0 05 (squint amblyopia) on the left 1 25 Ophthalmoscopy normal Perimetry on the right 10/2000 for white Concentric narrowing suspicion of a defect in the upper right quadrant Red was not perceived Left eye 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At the ventriculography under local anaesthesia the ventricles were found to be normal without any signs of dilatation or space filling lesions Pressure 80-140 mm of water The blood pressure rose during the procedure from 125/100 to 160/100 but immediately after fell to 130/95 9 + 13 ml of clear cerebrospinal fluid was evacuated

After the ventriculography the patient went blind On the following day he could perceive fingers On the third day after the ventriculography ophthalmological examination Visual acuity not determined mild choking of the discs without measurable prominence Visual field for fingers Left sided homonymous hemianopsia

The patient was discharged 9 days later with unchanged left sided homonymous hemianopsia

At follow up admission 6 months later ophthalmological examination showed the visual acuity to be 0 05 on the right and 1 0 on the left Ophthalmoscopy visual field for fingers on the right and perimetry on the left 3/2000 for white Normal Perimetry with Goldmann s perimeter Inferior quadrantic defect which was unchanged 2 years later

At that time EEG showed a moderately abnormal curve with focal changes posteriorly on the right

Case 7 (G20688) Diagnosis Chronic encephalitis

A woman aged 62 who for the past 6 months had been suffering from decreasing visual acuity diplopia frontal pressure headache with dizziness fa

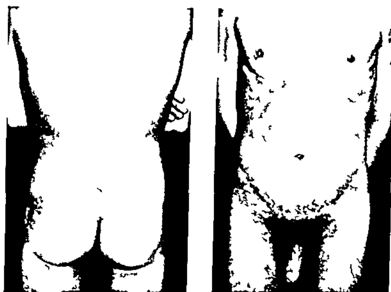


Fig 2

Pronounced skin lesions Patient IB) The lesions have a characteristic distribution being localized symmetrically predominantly on the lower trunk genital regian and upper thigh

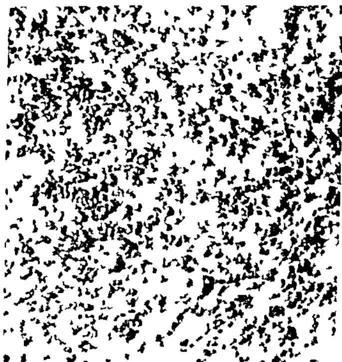


Fig 3

Close up view of skin lesion (Patient IB) showing the pin point to hemp seed sized dark(red) elevated elements

stitution must depend upon the length of time that the blood supply to the visual cortex is reduced and the underlying disease However as also emphasized by *Walsh* (10) it is usually good after ventriculography

Although the named pathogenesis may in many cases afford a satisfactory explanation of the development of bilateral homonymous hemianopsia several objections apply The blindness does not arise in connection with stereotactic operations for parkinsonism even though in this procedure far more air is insufflated than in ordinary ventriculography so that the pressure over the tentorium cerebelli ought to be even more increased than in ordinary ventriculography In the event of free flow between the supra and infra tentorial part of the ventricular system it seems difficult to conceive why incarceration should arise The free interval often reported between ventriculography and the appearance of visual disturbance makes it difficult to accept that bilateral homonymous hemianopsia should be due in all cases to incarceration in the tentorial notch with squeezing of the posterior cerebral arteries Direct injury to the visual pathways or visual cortex possibly with a haematoma cannot be considered very likely considering the symmetrical visual impairment. However in predisponed patients with an increased tendency to cerebral oedema the puncture may easily be imagined to give rise to oedema around the visual pathways or possibly of the visual cortex In 6 of the 8 present patients the diagnosis was encephalitis and as these patients are known to have an increased tendency to oedema the development of bilateral homonymous hemianopsia in these cases was perhaps due to oedema of the visual pathways around the trigone In the patient with hypertension there is reason to believe that the fall of blood pressure from 165/90 to 80/50 has been the cause In the patient with cerebral metastases there may possibly have been a question of incarceration although this could not be proved at autopsy

In 5 out of the 8 patients with bilateral homonymous hemianopsi the vision returned to normal in less than 10 days in one it had been restored at follow up 6 months later while in 2 no improvement had occurred at discharge 1 and ? months after the ventriculography

Among the 335 patients subjected to ventriculography there were apart from the 8 with bilateral homonymous hemianopsia another 7 with visual field defects (4 with unilateral homonymous hemianopsia and 3 with quadrantic anopsia) and 1? patients with other ocular symptoms viz blurred vision flittering before the eyes spots before the eyes micropsia and in one case transient unilateral pupillary dilatation

In the 7 patients with unilateral homonymous hemianopsia and homonymous quadrantic anopsia the prognosis was also good A lasting defect was recorded in only one case When first admitted this patient had hyperaemic discs with a prominence of 3 4 dioptres and at follow up 18 months later the discs were greyish white and atrophic



Fig 4
Corneal opacities (Patient IM) The opacities consist of whitish whorled streaks arranged in a vortex near the center of the cornea



Fig 5
Vascular abnormalities in the conjunctiva (Patient IB) The conjunctival vessels show some to tuosity and characteristic small focal varicosities and ampulliform and saccular dilatations

Ophthalmological examination 2 days after the ventriculography showed the visual acuity to be 0 67 on the right and 0 33 on the left Ophthalmoscopy un changed Visual field not determined

Ophthalomological examination 10 days later showed the same appearances as prior to the ventriculography Visual acuity 1 0 on the right and less than 0 67 on the left Ophthalmoscopy unchanged Visual field for fingers normal

Discussion

The present study is a retrospective one and accordingly carries certain inac curacies The patients were not questioned particularly about ocular symptoms after the ventriculographies so that perhaps only the most pronounced cases have been recorded Moreover the patients need not always have realized their blindness (Anton s syndrome) or have spontaneously mentioned their visual impairment

Bilateral homonymous hemianopsia has been described also after arterio graphy following anoxia head injuries air emboli and vascular occlusion (1 7, 12) The blindness may be the only finding although other ocular symptoms and systemic symptoms may co exist depending upon the underlying disease (8 11)

The *aetiology* of the sudden blindness following ventriculography is inter preted by most authors as cortical due to spasms or incarceration of the poste rior cerebral arteries where they cross the edge of the tentorium cerebelli at the incisural level (3 7 8) The greater part of the visual cortex is supplied by these arteries However its temporal part may also be supplied by a branch of the middle cerebral artery (9)

At the evacuation of cerebrospinal fluid and the subsequent insufflation of air into the ventricles it is imagined that a difference in pressure may arise between the supra and infra tentorial space with a risk of incarceration of the posteiror cerebral arteries in the tentorial notch The blindness often develops rapidly in relation to or immediately after the ventriculography When vision returns there may be before complete restitution a transitional period of unilateral homonymous hemianopsia a finding which might support the named pathogenesis (8)

Obscurations in the presence of elevation of intracranial pressure are inter preted in the same way as a consequence of intermittent disturbances of blood circulation in the visual cortex (2)

The fact that the cortical blindness may be accompanied by an impaired or abolished pupillary reaction to light must be assumed to be due to simultaneous spasms in the vessels supplying the brain stem The prognosis as to visual re

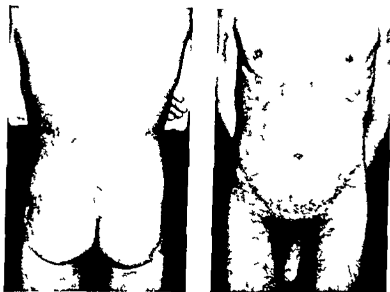


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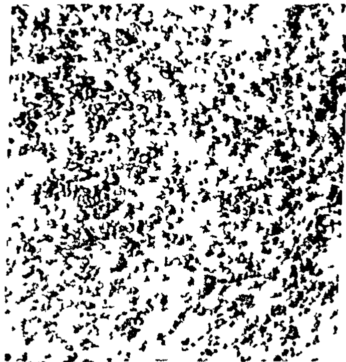


Fig 3

Close up view of skin lesion (Patient IB) showing the pin point to hemp seed sized dark(red) elevated elements

Københavns Amts Sygehus i Gentofte department of neurology (Heads E Fround en & P Thygesen) and department of ophthalmology (Heads P Kjer H W Larsen & V Larsen)

THE VALUE OF OCULAR FINDINGS IN THE DIAGNOSIS OF ANGIOKERATOMA CORPORIS DIFFUSUM (FABRY'S DISEASE)

BY

HANS OLAV CHRISTENSEN LOU ERIK HEIDENSLEBEN
and HANS-WALTHER LARSEN

In the past decades the so called inborn errors of metabolism have attracted great interest As a result our understanding of the underlying metabolic mechanisms have made great advances Still however a rational therapy has ensued in only a few diseases In the majority of metabolic diseases the physician has to content himself with making the diagnosis and giving genetic councelling

Early diagnosis and genetic councelling are of particular importance in Fabry's disease as it is an X linked recessive disorder with variable expressivity (*Opitz et al* 1965) in which affected family members can in most cases reproduce The first case reports on angiokeratoma corporis diffusum appeared in 1898 (*Fabry Anderson*) Although the disease has been known since then it was not until 1958 that the first report of an affected woman appeared in the literature (*Wallace*) Our increased knowledge of the clinical manifestations and the genetic biochemical and pathological mechanisms has resulted in the disease now being diagnosed more frequently Up to 1960 only about 50 cases were reported but since then more than 50 additional cases have been described The disease is not as rare as the literature might suggest since during the last few years *Jensen and Christensen Lou* 1966 and *Christensen Lou* 1970 found 24 cases in 4 families originating in the Copenhagen area

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heterozygote females and young males presenting only slight general manifestations

The presence of marked focal varicosities and ampulliform or saccular dilatations of the conjunctival vessels together with tortuosity of the vessels may also be of great diagnostic value in this disease

Retinal vascular tortuosity is considered to be of no diagnostic value if not present together with other manifestations of the disease

Characteristic vascular lesions in the conjunctiva are described in a female for the first time

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Such recurrent attacks were reported by 56 per cent of our patients *Thygeson* found herpes of the lips in no more than one third

Recurrence Rate

Recurrence was noticed in 61 per cent of the 109 cases Thus recurrence is seldom completely avoided

In the whole series each patient had on an average 3 4 attacks i e one first attack and 2 4 recurrences There was no significant sex difference (males 3 6 attacks females 3 1 attacks)

The number of attacks seemed to be the greatest in cases with first attack between the ages of 20 and 30 (on an average 7 8 attacks 13 patients against 3 5 attacks in 34 patients under 20) The frequency of attacks declines steadily after onset at the age of 30 presumably on account of decreasing observation periods

All the attacks seen within the period of investigation and all the attacks stated in the past histories were included as such

Intervals between Relapses

The time interval between the first and the second attack average 5 7 years (ranging from less than one year up to 47 years) Thus the patient can never feel safe against recurrence even after several years without such

The interval is independent of the patient s age at the time of the first attack

The interval between the first attack and the latest one recorded in cases with more than two attacks averaged 13 4 years (ranging from 2 to 30 years) Here too the interval was independent of the patient s age af the time of the first attack

Observation Period

The figures given for recurrence rate and time interval between attacks depended largely on the length of the observation period

The follow up was planned so as to obtain a sufficiently long observation period from the first attack This period was never less than 5 years often 5 12 years the series having been collected from a seven year period In 29 cases the observation period was still longer these patients having had their first attack before the beginning of the proper period of investigation

The observation period averaged 13 years

The attempt to obtain a long observation period had on the other hand the

We may thus probably be justified in concluding that no seasonal variations exist

Follow up

The follow up was in all cases carried out by the author himself Of the total series of 157 patients 109 were followed up 27 had died at this time Of these 21 would have been over 70 four in the 60ies and two in the 50ies at the time of the follow up if alive

The remaining 21 (13 per cent of the total series) were not followed up be cause the adress was unknown (3) the patient was away (6) admitted to another hospital (2) placed in a remand home (1) or failed to appear for examination (9)

The 109 patients followed up are described below

Bilateral Cases

Herpetic keratitis is usually a unilateral affection and relapses occur in the same eye

However, in ten of the 109 the affection came on simultaneously in both eyes and in one case there was keratitis in one eye and recurrence in the contralate ral eye Most of the patients with bilateral keratitis were children (six were under 10)

Only one patient experienced considerable impairment of vision of both eyes (a man aged 55)

Gunderson found 1 per cent bilateral cases among 221 patients *Laibson* 2 per cent (150 patients) *Sood* likewise 2 per cent (150 patients) *Thygeson* 9 5 per cent (200 patients) The 10 per cent bilateral cases in the present series is thus a high figure compared with those of previous statements

Primary Herpetic Keratitis

Primary keratitis was a likely diagnosis in seven of the 109 cases (follicular con junctivitis or vesicles on eyelid forehead nose or cheek simultaneously with first attack of herpetic keratitis) Four of these cases were bilateral

Thygeson (1956) found 4 5 per cent primary cases

Herpes of Lips

Recurrent herpes of the lips is often seen in patients with dendritic keratitis

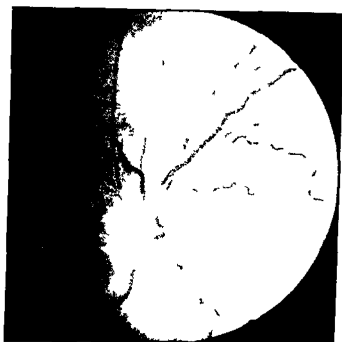


Fig 6
Left fundus of patient IH Some of the retinal veins show moderate tortuosity

of such lesions when pronounced must also be considered as highly characteristic of this disease

Retinal vascular abnormalities are especially seen in affected males In pronounced cases the abnormality is easily distinguished from normal vascular tortuosity In less pronounced cases however it is often difficult or even impossible to make this distinction

The present series confirms the diagnostic value of corneal opacities and conjunctival vascular abnormalities in Fabry s disease The occurence of corneal opacities is of special diagnostic value in the heterozygote females and young males Paradoxically the corneal opacities were found to be more pronounced in the heterozygote females than in males even if the latter usually showed more severe general symptoms and signs

Summary

In this study of Fabry s disease 11 out of 15 members of one family presented symptoms and signs of this disorder

It is pointed out that corneal opacities are of great diagnostic value in both

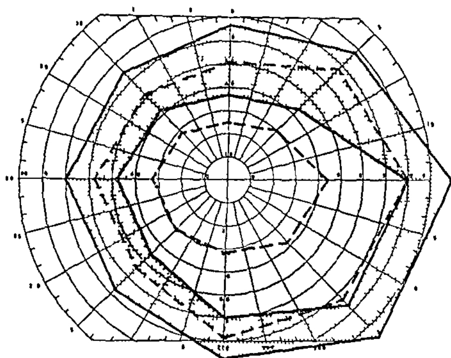


Fig 2

The variation observed with two different stimuli in kinetic perimetry obtained in a carefully standardized study of a large group of untrained normal subjects of different ages Redrawn from *Ferree et al*, 1931

The heavily stippled area illustrates the variation in perception thresholds for a stimulus subtending a visual angle of 1° at the eye The solid lines *enclosing this area* define the extreme limits (200 subjects) The lightly stippled area similarly illustrates the variation observed with a 0 17° stimulus in 150 subjects The broken lines define *the corresponding* extreme limits The rate of stimulus movement was not reported

experienced perimetrist who pays more attention to isopter shape than to size (*Traquair* 1939 *Lloyd* 1947 *Dubois Poulsen* 1952 *Harrington* 1964)

Isopter shapes

Rather than rigorously applying criteria of minimal permissible dimensions the experienced perimetrist thus aims to judge the shape of isopters This applies both to the primary distinction between normal and abnormal findings and to the further analysis of defective visual fields

The shapes of intermediary and peripheral isopters are most often loosely described as oval ovoid pear shaped etc The central isopters often appear more symmetrical but different authors diverge in opinion as to their shapes

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From the Department of Ophthalmology
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ON OBJECTIVE ANALYSIS IN KINETIC PERIMETRY

BY

L. FRISEN

The examination of the visual fields is of recognized value in the detection and localization of eye and brain disorders The methods of examination and the general understanding of their results have been improving for more than one hundred years It is not certain however that the ability to tell normal results from abnormal has made similar progress the primary pass or fail evaluation which determines the *yield of the examination is still largely subjective and* empirical Although subjective evaluation may be appropriate in the differentiation between normal and grossly abnormal visual fields it may be less suitable in the classification of borderline cases A correct evaluation of such cases requires precise information as to what should be considered normal This is at present mainly a matter of personal experience

Objective and meaningful descriptions of normal findings should be of assistance in subjective evaluation and might even allow the use of objective testing methods It is the aim of this paper to discuss various means of describing and analyzing the results of monocular kinetic perimetry the most common form of examination with particular reference to the shape of normal isopters

The conceptions pertaining to the visual fields and their examination are in part vaguely defined For this reason the first part of this paper aims to present a concise outline of the subject matter

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some stating that they are circular others that they are elliptical or oval Because of the successive change of isopter shapes from the center to the periphery within one and the same visual field and because of variation between and within subjects and examiners it is actually most difficult to define isopter shapes in unambiguous terms It also appears that there have been no published attempts to assess objectively the shapes of isopters in the sense of describing the relationship between neighbouring points on the curves On the contrary there is a prevalent attitude that the results of the visual field examination can only be judged subjectively (e g *Harrington* 1964) The evidence for this view does not appear to be available

The theoretical derivation of isopter configurations from present knowledge of morphology and physiology appears impossible The appalling number of factors involved is apparent already from the fact that a normal visual field finding presupposes integrity of the eye as well as the visual pathways and the visual cortex Therefore approaches to the definition of isopter shapes are probably best directed to the actual findings of visual field examinations

There are at least two apparently unexplored possibilities of improving the definition of normal isopter shapes The one aims to reduce between subject variation the other centres on a concept pertaining to shape characteristics

Under standardized conditions of examination the larger part of the total variation in results emanates from between subject variation (*Drance et al* 1966) A reduction of this contribution to the variation would improve the conventional numerical definitions of normal isopter shapes by providing narrower limits of normality One way of achieving this objective could be to correct for subject age A decrease of isopter dimensions with increasing subject age has been demonstrated recently (*Drance et al* 1967 *Fisher* 1968) An older subject as a rule signals perception of a given stimulus closer to the point of fixation than does a younger one The delay is attributable to increased reaction time decreased attention smaller pupillary area decreased transmission through the ocular media etc changes which affect the dimensions of isopters without contributing information as to the state of the retina the visual pathways or the visual cortex However such factors obviously are capable of variation also between subjects of one and the same age Therefore their influence should not be dealt with primarily by correcting for subject age but by individual correction with their actual magnitude This does not mean that the delay needs to be measured It is in principle much simpler to correct for these between subject sources of variation by individually adjusting the strength of the stimulus so that isopters having standard features are obtained It could be specified for instance that an intermediary isopter must always have say a temporal radius of 50 degrees of angle As a rule then an older subject would need a stronger stimulus than a younger one to present an isopter of identical temporal radius By using stimuli of individually appropriate strength it should

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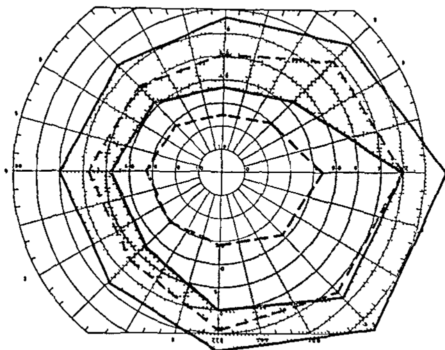


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plain the larger variation in threshold position in the upper part of the field (Fig 2)

The cartographic problem

Even the casual reader of geographical atlases has probably noticed the manifold possibilities of depicting a given geographical region One and the same global area may assume quite different appearances in different maps This is *due to the fact that there exists no single cartographic projection* that is able to represent without faults spherical surfaces in a plane On the contrary every cartographic projection involves characteristic distortions of linear angular and/or areal relationships in varying extents across the map Deformation is an unavoidable consequence of projection *This applies also to the standard cartographic projection of perimetry* the so called polar azimuthal equidistant projection The deformational properties of this projection have been analysed recently on the basis of a model of the visual space (*Frisen* 1970) It will suffice to note the following characteristics of deformation here

(I) Peripheral parts of an isopter outline are depicted on larger scales than parts lying closer to the center of the chart This tends to produce egg shaped projections of perfectly regular curves on the perimeter surface The more or less irregular shapes of normal isopters in visual field charts may well be compatible with regular shapes prior to the cartographic deformation Isopters of different sizes are differently affected

(II) If the isopter curves on the surface of the perimeter were symmetrical to a point on this surface they would lose this property during projection and would appear symmetrical only to a meridian The standard projection thus conceals centers of symmetry if such exist

(III) Angular and areal relationships that apply for isopters on the spherical surface are not preserved in the projection Distances between points on the curves on the sphere are represented proportionally only when they coincide with meridians

Thus the isopters of the visual field are complexly deformed during their projection to the plane perimetric chart Several valuable properties from the objective measuring point of view – notably those pertaining to possible conditions of symmetry – are lost in the chart

There are at least two quite simple ways to minimize or eliminate the cartographic deformation for the purpose of allowing the identification of simple mathematical functions fitting normal isopters (*Frisen* 1970) Both methods preserve certain properties of symmetry if such exist The one method is to change the customary point of fixation during perimetry so as to make the cen

The examination of the visual field aims to detect deficiencies in the discriminative ability of a subject within that space where he under steady monocular fixation can perceive light. Deficits of peripheral vision are manifested by contracted spaces and/or impaired perception within subspaces.

The examination usually concerns the photopic differential light sense measured as the ability to distinguish in various directions a light stimulus from a uniformly illuminated background. The very large number of possible variations with respect to physical characteristics of stimulus and background (size, shape, distance, colour, etc. cf. *Dubois Poulsen* 1952) need not be detailed here.

The visual space. The space within which a steadily fixating subject can perceive light monocularly is traditionally imagined as a sector of a sphere with its center in the nodal point of the eye. The maximal extent of this conical space is defined by the limits of functional retina. The maximal dimensions may be determined by noting the maximal angular distances relative to the eye and the line of sight at which a strong light stimulus is perceived. The cone may also be characterized by means of a spherical or plane section with the aid of a perimeter and a campimeter (tangent screen) respectively. Such a section, which forms a base of the visual space cone, defines the *visual field*.

Vision within the visual space may be characterized by threshold values for perception in selected directions. This is the basis of so called static perimetry. Kinetic perimetry, which is the subject of this paper, utilizes the fact that the ability to detect a stimulus improves with decreasing angular distances relative to the line of sight. The successive and monotonous change of threshold values allows a meaningful characterization in terms of directions of equal visual efficiency. The kinetic approach involves the use of weaker stimuli than those mentioned above to outline smaller visual cones. A section through such a cone produces a closed curve or *isopter*, which represents directions of equal visual efficiency.

An isopter does not normally convey any information as to visual function inside or outside the corresponding visual cone.

Kinetic examinations. Kinetic perimetry and kinetic campimetry both utilize a mobile light stimulus, which generally is moved from the periphery of the perimetric hemisphere or the campimetric plane towards the central point of fixation. This point is approached from several directions and in each case the subject has to acknowledge when he first perceives the moving stimulus. The point at which the stimulus is perceived is usually determined for eight or twelve equally spaced radii or meridians. The primary data (in terms of spherical or polar co-ordinates) are transferred to a visual field chart, where the points may be joined to approximate the isopter for that particular stimulus. The examination is then repeated with other stimuli so that the visual field finally is characterized by a number of isopters, usually two or three, which are examined with respect to abnormal features.

Depending on the number of isopters employed, there remains larger or smaller parts of the visual space between the nesting cones where visual function escapes representation. In practice, isopters do not allow an exhaustive characterization of the visual space. Unrepresented subspaces are usually screened with the aid of a supraliminal stimulus. One procedure consists of a sudden static exposure of a stimulus in unexpected positions within its isopter, requesting the subject to acknowledge perceived presentations. An alternative is to continue centripetal stimulus movement beyond the point of initial perception at the same time as the subject is asked to signal its possible disap

be possible to obtain closely similar isopters from different normal individuals i e the normal variability should decrease considerably Such a procedure would also tend to reduce the variation between examiners No information is lost by such an approach it is still possible and actually more simple than previously to compare the sensitivities of different individuals since a subject s sensitivity may be defined in terms of the physical characteristics of his appropriate stimulus for specified points in the visual field

Except for its lack of flexibility the main disadvantage of this approach is the need of access to sets of finely graduated stimuli These are not available in the present population of perimeters

The other approach depends on the widely accepted notion that is is possible to judge isopter shapes subjectively notwithstanding variation in linear dimensions Obviously this would be impossible if normal isopters did not share characteristics of shape The nature of such common characteristics is not known but the possibility should be considered that normal isopters except for random deviations belong to one and the same family of continuous mathematical functions and differ only with respect to function parameters It could be that all normal isopters belong to say the ellipse family of functions and differ solely as to axis characteristics and midpoint position If such a family of functions could be approximated by regression methods or if a common feature say symmetry with respect to a point[1] could be identified it would be possible to test objectively whether a given isopter *except for random deviations* displays normal characteristics or not The magnitude of function parameters is of secondary interest as emphasized above and with such a character testing approach normal limits no longer would be needed Another advantage is flexibility This should allow the use of present examination instruments

Because symmmetry with respect to a point is a characteristic of several families of mathematical functions of potential interest a search for isopter shape characteristics might benefit from an investigation of possible symmetry properties Symmetry properties of isopters are not so apparent in visual field representations however at least not in the case of intermediary and peripheral isopters This may be due to cartographic distortion consequent to the projection of primary data from the perimeter hemisphere to the plane visual field chart It is therefore necessary to consider the effects of projection

Incidentally it may be noted that the chart network in itself seems to induce visual illusion effects interfering with subjective appraisal of isopter shapes (*Aren & Frisen* unpublished) Possible properties of symmetry may be further obscured during perimetry by prominent facial reliefs and the varying and unsymmetrical covering of the cornea by the eye lids The latter factor may ex

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1) Symmetry with respect to a point means that the figure in question will coincide with its original position if it is turned less than 360° around the symmetry center

pearance. Irrespective of procedure a failure to perceive the stimulus denotes impaired vision. Any subspaces of wanting perception are then mapped out by moving the stimulus in various directions from the non seen area and noting the points of renewed perception.

The campimetric technique is used only in studies of the central parts of the visual field

Abnormal findings A localized reduction in visual efficiency appears to be the most important abnormality Generalized uniform impairments or so called concentric depressions also exist The latter are generally considered to be non specific Phenomena of photometric dysharmony may also occur (cf *Goldmann* 1945 *Dubois Poulsen* 1966) but seem to be little utilized in clinical work

The signs of localized defects are somewhat loosely classified as localized isopter depressions and scotomata. The differentiation is partly a matter of procedure partly a matter of topography Localized isopter depressions are commonly a manifestation of impaired vision within subspaces extending from the central parts of the visual space to its periphery Because reductions in visual efficiency result in an apparent centripetal displacement of perception thresholds a stimulus presented within a subspace of impaired vision will have to be moved closer than usual towards the point of fixation before perception occurs Hence the ensuing isopter will show an impression or localized depression corresponding to the directions and the degree of impaired vision Subspaces of impaired vision which do not engage the limits of the field are termed scotomata A scotoma often has such a size and shape as to fit between standard isopters The blind spot corresponding to the optic nerve head is a physiological scotoma

As a matter of fact the distinctions between scotomata and localized isopter depressions are of limited interest because all scotomata will show up in the form of localized depressions in suitably selected isopters Actually signs of retinal and visual pathway disturbances may nearly always be thought of in terms of localized isopter depressions Hence the ability to recognize abnormal isopters will largely determine the yield of the examination.

Methods of isopter characterization Standards of comparison

The results of the examination are obtained in the form of sets of co ordinates for points on isopter curves The sheer number of observations invites a reduction of the amount of data to be handled in characterizing isopters Two techniques are sometimes used for this purpose viz the calculation of the average isopter radius and the determination of the area enclosed by an isopter (e g *Ferree Rand & Monroe* 1930 1931 *Drance Berry & Hughes* 1967)

The average radius of an isopter is obtained simply by adding the angular distances between observed points and the point of fixation and dividing by the number of observations The resulting value does not convey any information as to the extent of the isopter in various directions It is thus of little use in diagnostic contexts This drawback applies also to the determination of the area enclosed by an isopter a technique which suffers from at least two additional disadvantages Firstly a large number of points must be observed to de

plain the larger variation in threshold position in the upper part of the field (Fig 9)

The cartographic problem

Even the casual reader of geographical atlases has probably noticed the manifold possibilities of depicting a given geographical region One and the same global area may assume quite different appearances in different maps This is due to the fact that there exists no single cartographic projection that is able to represent without faults spherical surfaces in a plane On the contrary every cartographic projection involves characteristic distortions of linear angular and/or areal relationships in varying extents across the map Deformation is an unavoidable consequence of projection This applies also to the standard cartographic projection of perimetry the so called polar azimuthal equidistant projection The deformational properties of this projection have been analysed recently on the basis of a model of the visual space (*Frisen* 1970) It will suffice to note the following characteristics of deformation here

(I) Peripheral parts of an isopter outline are depicted on larger scales than parts lying closer to the center of the chart This tends to produce egg shaped projections of perfectly regular curves on the perimeter surface The more or less irregular shapes of normal isopters in visual field charts may well be compatible with regular shapes prior to the cartographic deformation Isopters of different sizes are differently affected

(II) If the isopter curves on the surface of the perimeter were symmetrical to a point on this surface they would lose this property during projection and would appear symmetrical only to a meridian The standard projection thus conceals centers of symmetry if such exist

(III) Angular and areal relationships that apply for isopters on the spherical surface are not preserved in the projection Distances between points on the curves on the sphere are represented proportionally only when they coincide with meridians

Thus the isopters of the visual field are complexly deformed during their projection to the plane perimetric chart Several valuable properties from the objective measuring point of view – notably those pertaining to possible conditions of symmetry – are lost in the chart

There are at least two quite simple ways to minimize or eliminate the cartographic deformation for the purpose of allowing the identification of simple mathematical functions fitting normal isopters (*Frisen* 1970) Both methods preserve certain properties of symmetry if such exist The one method is to change the customary point of fixation during perimetry so as to make the cen

The examination of the visual field aims to detect deficiencies in the discriminative ability of a subject within that space where he under steady monocular fixation can perceive light Deficits of peripheral vision are manifested by contracted spaces and or impaired perception within subspaces

The examination usually concerns the photopic differential light sense measured as the ability to distinguish in various directions a light stimulus from a uniformly illuminated background The very large number of possible variations with respect to physical characteristics of stimulus and background (size shape distance colour etc cf *Dubois Poulsen 1952) need not be detailed here*

The visual space The space within which a steadily fixating subject can perceive light monocularly is traditionally imagined as a sector of a sphere with its center in the nodal point of the eye The maximal extent of this conical space is defined by the limits of functional retina The maximal dimensions may be determined by noting the maximal angular distances relative to the eye and the line of sight at which a strong light stimulus is perceived The cone may also be characterized by means of a spherical or plane section with the aid of a perimeter and a campimeter (tangent screen) respectively Such a section which forms a base of the visual space cone defines the *visual field*

Vision within the visual space may be characterized by threshold values for perception in selected directions This is the basis of so called static perimetry Kinetic perimetry which is the subject of this paper utilizes the fact that the ability to detect a stimulus improves with decreasing angular distances relative to the line of sight. The successive and monotonous change of threshold values allows a meaningful characterization in terms of directions of equal visual efficiency The kinetic approach involves the use of weaker stimuli than those mentioned above to outline smaller visual cones A section through such a cone produces a closed curve or *isopter* which represents directions of equal visual efficiency

An isopter does not normally convey any information as to visual function inside or outside the corresponding visual cone

Kinetic examinations Kinetic perimetry and kinetic campimetry both utilize a mobile light stimulus which generally is moved from the periphery of the perimetric hemisphere or the campimetric plane towards the central point of fixation This point is approached from several directions and in each case the subject has to acknowledge when he first perceives *the moving stimulus The point at which the stimulus is perceiv*ed is usually determined for eight or twelve equally spaced radii or meridians The primary data (in terms of spherical or polar co ordinates) are transferred to a visual field chart where the points may be joined to approximate the isopter for that particular stimulus The examination is then repeated with other stimuli so that the visual field finally is characterized by a number of isopters usually two or three which are examined with respect to abnormal features

Depending on the number of isopters employed there remains larger or smaller parts of the visual space between the nesting cones where visual function escapes representation In practice isopters do not allow an exhaustive characterization of the visual space Unrepresented subspaces are usually screened with the aid of a supraliminal stimulus One procedure consists of a sudden static exposure of a stimulus in unexpected positions within its isopter requesting the subject to acknowledge perceived presentations An alternative is to continue centripetal stimulus movement beyond the point of initial perception at the same time as the subject is asked to signal its possible disap

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Concluding remarks

The conventional methods of isopter representation certainly introduce difficulties in objective evaluation in that i a symmetry properties if such exist are concealed Attempts to describe quantitatively isopter shapes therefore should benefit from changing the customary representation The alternatives i e the correction of cartographic deformation during analysis or the use of procedures of spherical geometry would be almost impossible to handle in practice without the aid of computers

If well fitting mathematical functions or properties of symmetry could be identified and studies of intermediary isopters obtained with parapolar fixation indicate that they appear to display point symmetry (Fig 3 see also *Frisén* 1970) it would be possible to analyse individual visual field findings objectively with respect to isopter shapes and uniformity of variation Limits of normal variability would no longer be needed Space occupying normal records often stored for possible future reference could be replaced with a few notes of relevant characteristics Rigorously standardized instrumentation would not be needed Furthermore evaluations of this type might permit the hitherto impossible definition of defect magnitudes in terms of departures from expected values and they might possibly disclose hitherto unknown types of defects What is perhaps most important is that knowledge of normal isopter shapes appear to be a requisite to the construction of meaningful and sensitive screening proce

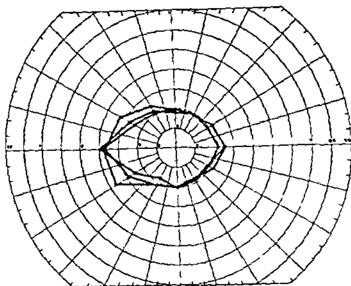


Fig 1

Observed values for different diameters within an intermediary isopter of a normal emmetropic subject aged 27 Data from three consecutive determinations are superimposed in the chart to illustrate the normal within subject variation under standardized conditions

A modified Zeiss Jena arc perimeter was used The instrument was equipped with integral arc illumination ensuring a constant stimulus/background brightness contrast (*Frisen* 1969) and a synchronous motor mechanism ensuring constant rates of stimulus movement The rate used here was 2 9°/s On perceiving the stimulus the subject actuated a micro switch interrupting the motor current and applying a braking moment to the rotor This arrangement prevents the reaction time of the examiner influencing the result The results were recorded on a built in punch type chart recorder in the scale 1° = 1 mm The perimeter also incorporates devices for projecting a fixation target to any desired *point within the 20° parallel circle* Here the target was placed in the pole

The two endpoint of each diameter were determined sequentially i e the arc was not rotated to a new position until both endpoints were determined The rotation was carried out in such a manner as to preclude learning and fatigue bias

by a single value (e g *Ferree et al* 1931 *Goldmann* 1945 *Chamlin* 1959) of doubtful applicability On the other hand knowledge of the limits of normal variation is of little use because the latter are wide enough to accept substantial local depressions What is needed is a method that *in the presence of random variability* is able to single out isopters where neighbouring points on the curve show an abnormal relationship to each other i e a method for the detection of aberrations from normal shape This of course is the guiding principle of the

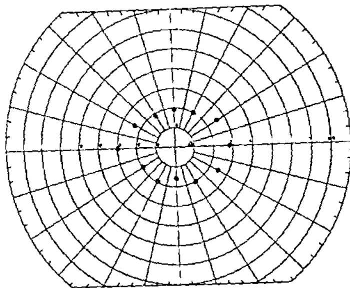


Fig 3

Observed values for different diameters within an intermediary isopter obtained with parapolar fixation The point of fixation (the triangle) was selected so as to make the presumed center of symmetry coincide with the pole It was tentatively presumed that this point would be situated midway between the point of fixation and the blind spot midpoint (cf *Frisen* 19/0) Except for the changed point of fixation the experimental conditions and the subject were identical with those described in the caption to Fig 1

These bservations and similar data from an additional nine experiments on diffe rent normal subjects were subjected to a statistical analysis with respect to departures from point symmetry (diametral symmetry) If an isopter displays point symmetry (except for random deviations) a certain expected value of diameter differences will be independent of the direction of the diameter (M *Frisen* 19 0) A two way analysis f variance did not disclose any statistically significant departures from symmetry with respect to the selected center

dures Such procedures would be of great value becaus of the time consum ing and exacting nature of conventional perimetric examinations (*Lynn* 1962)

Summary

Previously described methods of visual field isopter characterization are review ed. These methods give normal limits that are too wide to be of practical value furthermore they do not as desired describe the normal relationship between

fine accurately the enclosing curve if only a small number of points are determined and connected by straight lines, as is usually the case the resulting polygon will enclose a smaller area than the real isopter Secondly the measurement is not valid if it is performed on the standard visual field chart constructed on the principle of equidistant azimuthal polar projection (*ten Doesschate* 1947 *Frisen* 1970) This particular type of projection is not cartographically equivalent i e the areas enclosed by isopters in the chart are not proportional to the areas enclosed by the isopters on the perimetric hemisphere Valid determinations of area require the use of other types of charts (*ten Doesschate* 1947)

There is a large range of normal values for the area enclosed by a standard isopter (i e an isopter obtained by a standard stimulus) in the standard chart (*Drance et al* 1967) and isopters with subjectively discernible local depressions may well fall within normal limits This applies also to the average isopter radius which naturally is highly correlated to the enclosed area (*Drance et al* 1967)

Because the extent of an isopter in various directions is of crucial diagnostic importance isopters are in practice seldom or never subjected to data reducing handling but remain characterized by the co ordinates for observed points Observed data may then be compared with reference data tabulated separately (e g *Ferree et al* 1931) or inlaid in the visual field chart (e g *Chamlin* 1968) The sources of reference isopters in commercial charts are often unknown The technique of comparing the two visual fields of one and the same individual requires information as to which one should be considered normal

The procedure of point to point comparisons between observed data and reference data is mainly applicable to the peripheral part of the visual field where the variation is considerably smaller than in central and intermediary parts (*Ferree et al* 1931 *Dubois-Poulsen* 1966) Unfortunately peripheral isopters are generally considered less valuable from diagnostic points of view than non peripheral ones (*Traquair 1939 Blum Gates & James 1959*)

There are a large number of variables which influence the dimensions of isopters and cause variation between subjects Some of these variables also produce variation within subjects i e repeated examinations of one and the same subject do not give identical results (Fig 1)

The result is also influenced by variation within and between examiners The nature of the sources of variation and possible means of minimizing their influence need not be detailed here (see *Lynn* 1969) Even under the most carefully standardized conditions of examination there remains a considerable number of uncontrolled or imperfectly controlled sources of variation These combine to produce normal limits of a remarkable magnitude (Fig 2)

The distressing degree of normal variability is well reflected by the fact that the standards of comparison seldom or never indicate the extent of permissible variation The standards are almost exclusively meridian for meridian defined

ter of symmetry of the isopter under investigation coincide with the perimeter pole i e using parapolar fixation This will minimize the effects of the varying deformation across the chart and it allows the use of parameters of diametral symmetry The other method consists of the use of another familiar projection viz the central tangential or gnomonic projection sometimes used in the mapping of central parts of the visual field This projection can be regarded as a simple extrapolation of the rays defining the visual cones i e it is equivalent to plane rather than spherical sections of the visual cones It appears unnecessarily complicated to characterize the visual cones by means of their intersections with a spherical surface (as is the case in perimetry) because the configurations of the curves of intersection i e the isopters will be difficult to grasp and to describe once they deviate from circles The cones could be characterized directly by means of plane sections for possible ease of analysis The equivalents of plane sections are easily obtained by central tangential projection of perimetric data The cartographic deficiencies of this projection (cf *ten Doesschate* 1947) may be ignored in these contexts because the problem is in fact not a cartographical one

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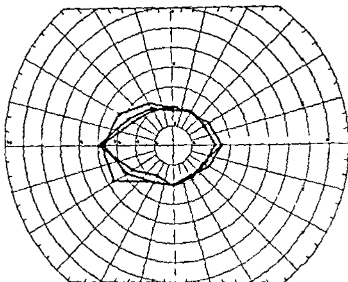


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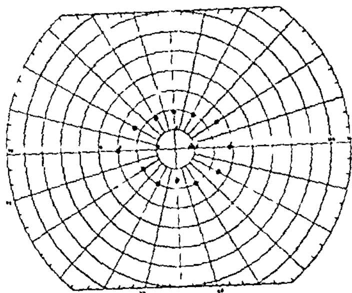


Fig 8

Observed values for different diameters within an intermediary isopter obtained with parapolar fixation The point of fixation (the triangle) was selected so as to make the presumed center of symmetry coincide with the pole It was tentatively presumed that this point would be situated midway between the point of fixation and the blind spot midpoint (cf *Frisen 1970*) Except for the changed point of fixation the experimental conditions and the subject were identical with those described in the caption to Fig 1

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Previously described methods of visual field isopter characterization are reviewed These methods give normal limits that are too wide to be of practical value Furthermore they do not as desired describe the normal relationship between

years (table IV) A similar observation period for the total series gave only an average of 1 4 attacks (table III)

Thus the IDU treated had *a greater number of relapses*

Recurrence after Steroid Therapy

Steroid therapy was mainly employed in cases of corneal oedema and impending *metaherpetic development*

Recurrence seemed to be more frequent after steroid treatment than after no treatment (table IV) This difference may however be accountable for by longer observation of the steroid treated The increased number of relapses corresponds in fact approximately to the longer observation period (cf table III)

In other words the steroid treatment has not been shown to cause any significant alteration of the recurrence rate

Table IV

Number of attacks considered in relation to therapy (IDU steroid iodine cauterisation) 109 patients with herpetic keratitis

therapy	number of attacks 1	2	3	4	5	>5	aver number of attacks	obs period	number of patients
IDU	18	16	6	4	5	7	4 0	12 2	56
no IDU	25	10	10	1	2	5	2 7	13 8	53
IDU	27	18	3	[illegible]	2	4	[illegible] 5	5 6	56
steroid	1	10	2	4	2	8	4 7	14	38
no steroid	31	16	14	1	5	4	[illegible] 6	1[illegible] 4	71
cauterisation	7	19	15	4	6	11	3 9	14 4	82
no cauterisat	16	7	1	1	1	1	1 9	8 5	27
steroid and or IDU	[illegible]	19	7	4	6	12	4 1	12 5	73
neither steroid nor IDU	18	7	9	1	1	0	1 9	13 8	36
metaherpetic	15	1	5	3	4	9	4 1	13 9	53
not metaherp	8	9	11	2	3	3	[illegible] 7	1[illegible] 0	5[illegible]
Total	43	[illegible]	16	5	7	1[illegible]	3 4	13 0	109

r k ned from the point of time at which the first IDU treatment was instituted

disadvantage that 17 per cent of the patients had died at the time of the follow up and therefore had to be ruled out

The number of relapses was seen to depend largely on the time of the follow up as shown in table III With an observation time of 5 6 years the average number of attacks was no more than 1 4 (0 4 relapses) An observation period of 18 years, on the other hand disclosed on an average 7 attacks (6 relapses)

Observation of more than 5 attacks in the same patients required an observation period exceeding 11 years

After an observation period of more than 18 years only one recurrence free case was seen (a man aged 68 observed for 35 years)

The conclusion may be drawn that a very long observation period is required before it is possible to pronounce approximately on the recurrence rate The figures show that the chance of recurrence is great provided the observation period is sufficiently long Recurrence may be experienced after a recurrence free interval of many years

Recurrence after IDU Therapy

The number of attacks among patients treated with IDU was greated (average 4 0) than among those never given IDU

IDU therapy was introduced later than the other treatments The mean observation period was therefore shorter for the IDU treated The proper increase of relapses after IDU must therefore be higher than the figures suggest

By including solely the period after the first IDU treatment had been prescribed on an average 2 5 attacks were found after an observation period of 5 6

Table III

Number of attacks considered in relation to length of observation period 109 patients with herpetic keratitis

Obs period in years	aver number of attacks	number of patients
5– 6	1 4	23
7– 8	1 9	15
9–10	2 2	25
11–12	3 6	17

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International Society of Geographical Ophthalmology

Following the First International Congress on Regional Ophthalmology held in Yellowknife, N W T Canada, in June 19 0 an *International Society of Geographical Ophthalmology* was formed.

The co opted executive commitee formed was composed of 1 professor Ida Mann Nedlands West Australia 2 Professor M E. Weigelin, Institute of Experimental Ophthalmology Bonn, Germany 3 Dr Alberto Ciancia Buenos Aires Argentina 4 Dr Abraham Kornzweig New York City U S A 5 Dr Wm John Holmes Honolulu Hawaii Secretary 6 Dr E Cass Northwest Territories Canada President

It is proposed to have two research centers one in Yellowknife N W T Canada and one in Bangkok As much information as possible will be collected on all work already done on Geographical Ophthalmology in order to ascertain the total factors causing ophthalmic conditions and their distribution throughout the world It s hoped it will be possible to find out the areas where research is inadequate or non existant and to encourage research where necessary

It is proposed that the next meeting be held in two years time either in Israel or in Auckland A bulletin shall be published from time to time giving papers on research in Geographical Ophthalmology

The yearly subscription shall be ten dollars per annum to get the society incorporated and send to mr Mark de Weerdt Q C P O Box 939 Yellowknife N W T Canada

10.-13 Juni 1971 14 Jahreshauptversammlung der Österreichischen Ophthalmologischen Gesellschaft in Lin

Anfragen und Anmeldungen *sind an Doz Dr W Funder erbeten* Wiener Medizinische *Akademie* fur arztliche Fortbildung Spitalgasse 7 A *1090* Wien IX Österreich Sprechzeit Vortrage 10 Minuten Mitteilungen und Demonstrationen 6 Minuten Anmeldeschluss fur wissenschaftliche Beitrage *1 Mar 1971*

Course in Retinal Detachment

The Retina Service Massachusetts Eye and Ear Infirmary will sponsor the 9th Annual course in Retinal Detachment on May 20 21 and 22 1971 The curriculum will include lectures covering the fundamentals of fundus diagnosis pathogenesis and modern methods of treatment of detached retinas Tuition is $ 125 for practitioners Residents $ 0 upon application from Department Head Checks are payable to Massachusetts Eye and Ear Infirmary and should be sent to Ronald C Pruett M D Retina Service Massachusetts Eye and Ea Infirmary 243 Charles Street Boston Massachusetts 02114

VARIA

SUPPLEMENTA

neighbouring points on isopter curves Possible approaches to the quantitative definition of the shapes of normal isopters amidst random variability are discussed and illustrated

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years (table IV) A similar observation period for the total series gave only an average of 1 4 attacks (table III)

Thus the IDU treated had a greater number of relapses

Recurrence after Steroid Therapy

Steroid therapy was mainly employed in cases of corneal oedema and impending metaherpetic development

Recurrence seemed to be more frequent after steroid treatment than after no treatment (table IV) This difference may however be accountable for by longer observation of the *steroid treated* *The increased number of relapses corresponds* in fact approximately to the longer observation period (cf table III)

In other words the steroid treatment has not been shown to cause any significant alteration of the recurrence rate

Table IV

Number of attacks considered in relation to therapy (IDU steroid iodine cauterisation)

109 patients with herpetic keratitis

therapy	number of attacks 1	2	3	4	5	>5	aver number of attacks	obs period	number of patients
IDU	18	16	6	4	5	7	4 0	12 2	56
no IDU	25	10	10	1	2	5	2 7	13 8	53
IDU	27	18	3	2	2	4	2 5	5 6	56
ste id	12	10	2	4	2	8	4 7	14	38
no steroid	31	16	14	1	5	4	2 6	12 4	71
cauterisati n		19	15	4	6	11	3 9	14 4	82
no cauterisat	16	7	1	1	1	1	1 9	8 5	27
ster d and/or IDU	[illegible]	19	7	4	6	12	4 1	12 5	73
neither steroid n r IDU	18	7	9	1	1	0	1 9	13 3	36
metaherpet c	15	17	5	3	4	9	4 1	13 9	53
not metaherp	8	9	11		3	3	2 7	12 0	56
T tal	43	[illegible]	16	5		12	3 4	13 0	109

reck ned fr m the point of time at which the first IDU treatment was inst tuted

Recurrence after Iodine Cauterisation

Local iodine cauterisation on the dendritic process is the earliest one of the treatments instituted The mean observation period was therefore longer for the patients thus treated than for the others

The longer observation period can fully explain the apparently increased recurrence rate The recurrence rate could not be demonstrated to have altered under the influence of cauterisation

Some of the cauterized patients had been treated with IDU and/or steroid (table V) Unfortunately it was impossible to tabulate groups subjected to any one pure treatment because the number of cases within each of such groups would be too small in the series under review

The patients given neither IDU nor steroid had fewer relapses The recurrence rate seemed to be unaltered after iodine cauterisation

Recurrence after Metaherpetic Development

In 53 of the 109 patients the lesion penetrated into deeper layers at some time or other having therefore been characterized as metaherpetic in the case record

The mean observation period was a little longer for the metaherpetic cases The recurrence rate seemed not to be significantly raised among these compared with the more superficial cases (table IV)

Visual Impairment

Two of the 109 patients with herpetic keratitis were subjected to corneal transplanation The degree of visual impairment therefore could not be estimated in these two cases

Table V

Treatment of 109 patients with herpetic keratitis The figures represent the percentage numbers of patients given the combined treatment concerned (56 IDU treated 38 steroid treated and 82 cauterized)

	also subjected to		
	IDU	Steroid	Cauterisation
treated with IDU	–	38	54
treated with steroid	55	–	79
treated by cauterisation	37	37	–

Table VI
Visual acuity at follow up of 107 patients after dendritic keratitis (Best vision stated in 11 bilateral cases)

	< 6/60	< 6/36	< 6/24	< 6/18	< 6/12	< 6/9	< 6/6	≥ 6/6	no of pts
IDU	3	2		1	8	11	11	21	54
no IDU	3	1	3	3	6	6	8	23	53
steroid	4	2	2	1	6	7	6	8	36
no steroid	2	1	9	3	3	10	13	36	71
cauterisation	4	2	5	3	8	13	15	31	81
no cauterisation	2	1	0	1	1	4	4	13	26
steroid and/or IDU	5	3	3	2	7	12	13	26	71
neither steroid nor IDU	1	0	2	2	2	5	6	18	36
metaherpetic	6	3	4	1	7	8	10	12	51
not metaherpetic	0	0	1	3	2	9	9	32	56
Total	6	3	5	4	9	17	19	44	107

In the 11 bilateral cases only the eye with the least visual impairment i e the eye used by the patients in practice was tabulated

The visual acuity recorded is that obtained with the best possible correction but without use of stenopeic hole or split

In eight cases the visual impairment was due not only to corneal opacity after previous herpetic keratitis but also to senile central retinal degeneration or cataract In these cases the visual impairment due to the corneal defect alone was roughly estimated The visual acuity recorded was therefore better than that measured at the follow up

Astigmatism was frequent especially among patients with diffuse corneal opacity and considerable visual impairment (35 of the 107 patients had astig matism $\geq$ 1 dioptre 18 $\geq$ 2 dioptres and 5 $\geq$ 4 dioptres)

The visual acuities at the follow up are shown in table VI All the patients are supposed to have had a normal vision (6/6) before the first attack of herpe tic keratitis

Only six out of 107 had under 6/60 at the follow up

Visual Impairment after IDU Therapy

At the follow up there was no difference in visual acuity between the IDU treated and those given no IDU (table VI) in spite of the fact that recurrences were more frequent among the former

Accordingly we may conclude that the individual attacks are less harmful to the patient s vision when IDU is given but that the changes of fresh relapses are greater The final visual impairment is of the same order for IDU treated and untreated

Visual Impairment after Steroid Therapy

The steroid treated had a poorer vision than the non steroid treated This may be due to the fact that steroid was preferably given to patients whose disease had reached a bad phase being under metaherpetic development with visual impairment before the treatment was started We therefore cannot draw defi nite conclusions concerning the effect of steroids on the vision

The patients given neither IDU nor steroid experienced the least visual im pairment

Visual Impairment after Iodine Cauterisation

In 81 iodine cauterized patients the final degree of visual impairment was ap proximately the same as in 26 non cauterized Cauterisation is probably mainly performed in the fairly grave cases and the cauterisation itself may tend to

augment cicatrisation if deep One aims however at not penetrating below the level of Bowman s membrane

Cauterisation could not be demonstrated to have any deleterious effect on the visual acuity On the contrary if the cauterized cases may be regarded as particularly grave the cauterisation had a vision preserving effect if anything

Visual Impairment after Metaherpetic Development

As might be expected the mean visual impairment was much greater after metaherpetic development than in the cases where the herpetic keratitis remained superficial (table VI)

Discussion

In the present study it was aimed at obtaining an observation period sufficiently long to give an impression of the true recurrence rate The mean observation period was 13 years The affection recurred in 61 per cent of the cases with on an average 3 4 attacks per patient in the total series

The observation periods are shorter or unknown in previously published studies and the recurrence rates found are considerably lower than in the present series

Davidson noticed recurrence in 16 per cent (51 patients) *Caperrucci* in 15 per cent (obs 6 7 months IDU treated) *Carroll et al* in 26 per cent not previously affected with dendritic keratitis and in 43 per cent with previous attack (2 years of observation, 159 patients)

Gilkes found recurrence in 40 per cent (159 patients) *Kaufman* (1963) and *Gordon* in one third of IDU treated *Patterson* in 10 per cent (84 patients obs 18 months) *Sood* in 11 per cent (150 patients obs period unknown) *Laibson* 21 per cent (100 patients obs less than 1 year) *Thygeson* 40 per cent (?00 patients) *Thomas et al* 15 per cent (11? patients)

Gundersen found on an average 2 1 attacks per patient (??1 patients retrospective investigation and further 3 /2 years of observation, the mean obs period unknown)

The higher recurrence rate in the series under review is probably mainly due to the longer observation period as it could be shown that the observation period has an influence on the recurrence rate found and that relapses may occur very long after the first attack

However geographic seasonal and therapeutic factors may also influence the recurrence rate (*Laibson*)

In the present study IDU treatment was seen to involve an increased risk of recurrence

Patterson saw recurrence in seven out of 43 IDU treated against in only one

In the 11 bilateral cases only the eye with the least visual impairment i e the eye used by the patients in practice was tabulated

The visual acuity recorded is that obtained with the best possible correction but without use of stenopeic hole or split

In eight cases the visual impairment was due not only to corneal opacity after previous herpetic keratitis but also to senile central retinal degeneration or cataract In these cases the visual impairment due to the corneal defect alone was roughly estimated The visual acuity recorded was therefore better than that measured at the follow up

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tabolites will appear whose properties are superior to those of IDU preferably such as reduce the chance of recurrence

The degree of visual impairment after dendritic keratitis constitutes a practical measure of the functional damages caused by the disease In the present study it has therefore been employed as a measure of the effect or failing effect of the therapy However the visual impairment also depends on the site of the keratitis (most pronounced at central localisation)

It will therefore be appropriate to report other parameters from the follow up This will be done in some future papers (corneal opacity vascularisation Fischer Schweitzer s fluorescein pattern permanent holes in the precorneal film vital staining and corneal sensitivity)

Summary

The above study was based on a series of patients with dendritic (herpetic) keratitis referred within a seven year period to an ophthalmic out patient department *The series comprised 157 patients of whom 109 were followed up*

The incidence was calculated at 1 196 among all ophthalmic patients with a male preponderance (59 per cent males) The age distribution at first attack showed that the majority were children or patients between the ages of 40 and 50 10 per cent were bilateral and 6 per cent probably primary No seasonal variations were detected

Relapses were frequent (in 61 per cent) with an average of 3 4 attacks per patient The interval between the first and the second attack averaged 5 7 years and that between the first and the latest one recorded 13 4 years (mean observation period 13 years)

The recurrence rate was higher for the IDU treated than for the non IDU treated but the recurrences seemed to run milder courses the final visual impairment being of the same degree in the two groups

Steroid therapy apparently caused graver visual impairment

Iodine cauterisation seemed to have no influence on the recurrence rate nor add *to the visual impairment*

Acknowledgement

The bove study was aided by a grant from *Cykelhandler P Th Pasmussen og hustru Ilna Pa m s ns Min lelegat*

Mrs S *Meul ig a ht* secretary undertook inquiries at National registration offices an l rgan ze l ummon ng of patients for the follow up

out of 41 placebo treated *Davidson Burns* and *Hughes* suggested the possibility of earlier recurrence after IDU while *Carroll et al* found no difference

Previous investigations have been concentrated particularly on the question whether IDU can shorten the active phase of herpetic keratitis

If a shortened period of treatment implies less pain less cicatrisation of the cornea less visual impairment and a reduced chance of recurrence the treatment is ideal

However the present investigation gave results suggesting that IDU adds to the chance of recurrence On the other hand the treatment did not entail a poorer visual prognosis Thus the numerous fairly short relapses seemed not to be more dangerous than the spontaneous course with fewer but more protracted attacks

The different forms of therapy are difficult to compare because they may be given at different indications dependent on the severity of the affection

IDU has however been given as a routine since the introduction of the drug

A steroid has often been given in particularly difficult cases The apparently poor final visual response to this treatment is therefore difficult to assess

The series under review presented no cases of iatrogenic chronic dendritic kerato uveitis in Thygeson s sense nor fatal cases with secondary bacterial or mycotic infection

Cauterisation with iodine seemed not to increase the risk of recurrence or the visual impairment

Several patients of the present series were treated with two or more drugs If series subjected to only one therapy each were available the differences would probably stand out more clearly The IDU treated groups would then presumably show a greater number of relapses and the steroid treated a more pronounced visual impairment

A rational therapy against dendritic keratitis is difficult to suggest on the basis of the results achieved from the present investigation

*IDU treatment must be warned against owing to the increased chance of re*currence possibly due to the cytotoxic effect of the drug IDU should perhaps be given for a short period only

The risk involved by steroid treatment has been suggested in this paper and borne out by *Thygeson* among others

The conventional cauterisation seems not to add to the risk of recurrence or visual impairment

In agreement with *Davidson* we may recommend treatment of dendritic keratitis with IDU for one week If this treatment does not cure the affection completely the remaining active area should be subjected to iodine cauterisation The IDU treatment has a definitely rational basis It is however no ideal therapy

It is to be hoped – and may probably be expected – that other virus antime

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MICROPUNCTATE FLUORESCEIN VITAL STAINING OF THE CORNEA

BY

M S NORN

Vital staining of the cornea with fluorescein is employed for controlling among other things the state of the cornea of contact lens wearers the fluorescent areas being assessed in cobalt filtered light in the slit lamp

Fluorescein only penetrates into the corneal epithelium at the sites of interrupted continuity of the epithelial surface The dye thus discloses lesions of the corneal epithelium

A peripherally localized fluorescein stained corneal area may be due to the contact lens being too curved with the result that the edge of the lens or its intermediary curve injures the cornea

If, on the other hand the stained area is found centrally the lens may be too flat thus directly eroding the central corneal zone or it may on the contrary be so greatly curved as to cause deficient ventilation of tear fluid and consequently a tendency to central oedema of the cornea In the stated cases the lens should be modified

In some instances a diffuse fluorescein staining is seen in the form of numerous minute dots This phenomenon is not infrequently observed during the adaptation period and is possibly accountable for by a too liberal adaptation schedule

In some eyes we see only very few minute fluorescein dots on the cornea In principle such dots must be regarded as minor lesions of the corneal epithelium

Received May 17th 1969

These may equally well as larger erosions become the point of entrance of bacteria fungi and virus

The more closely the cornea is inspected for fluorescein staining the more often such is found The question is whether fine punctate fluorescein staining may be a physiological phenomenon and whether a certain minimum fluorescein staining ought to be tolerated in practice as inevitable *also in contact lens wearers*

In an previous study (*Norn* 1964 A) I showed that punctate fluorescein staining may be seen in normals on the palpebral conjunctiva (in 21 per cent) and on the *caruncle* in the latter area presumably only in the hair follicles

No proper fluorescein staining was detectable on the cornea of normals or of patients with corneal degeneration or conjunctivitis

Using a special careful technique of examination it is however possible to detect small fluorescein stained dots even in normal eyes In the *present paper* the phenomenon is termed micropunctate fluorescein staining

Method

As vital stain is *used fluorescein* at a concentration of 0 125 % or 1 % the latter concentration in combination with 1 % *rose* bengal to be able to compare the *results* of these two vital stains *differing in principle*

One of the following three dye solutions is used

1) 0 125 % *fluorescein* rendered isotonic with NaCl with no *preservative* added
2) A *fluorescein* oxibuprocaine *mixture* acc to *Fenton* containing 0 125 % fluorescein 0 4 % oxibuprocain *chloridum* (NFN) (novesin Wander an anaesthetic) and 0 0025 % phenylmercuric nitrate as preservative and NaCl for isotonia
3) A fluorescein rose bengal *mixture* 50 mg *fluorescein*, 50 mg rose bengal 45 mg NaCl and distilled water to 5 g with 0 001 % phenylmercuric nitrate added

The pH values of these dye *solutions* range from 6 37 to 7 70

The dye solution is instilled into the inferior conjunctival fornix from a needle mounted tube yielding a drop of 0 01 ml (*Norn* 1964 B)

The patient blinks a few *times* after which the *cornea* is observed in cobalt filtered light in the slit lamp The examination is repeated after 1 2 minutes to record the finest punctate staining which may have been concealed by staining of the precorneal *film* on the first examination

Examination is repeated until the colour of the precorneal film is so pale that is can no longer be suspected to interfere with a possible *staining* of the corneal epithelium

The minute fluorescein stained dots are counted and the number entered in a table

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Table I

Age distribution of normals presenting micropunctate fluorescein staining

Age	fluorescein 0.125 %		fluorescein 1 % and rose bengal 1 %	
	% stained	number exam	% stained	number exam
< 40	4	42	0	10
40–49	13	65	67	6
50–59	20	106	82	22
60–69	19	117	83	6
≥ 70	22	81	40	5
Total	17	411	73	49

Table II

Micropunctate fluorescein staining of normal eyes. Sex distribution and dependence on dye solution. The figures indicate the percentage numbers of subjects whose eyes were stained

	women	men	Total	number of eyes examined
0.125 % oxibuprocaine fluorescein	16	17	16	340
0.125 % fluorescein	24	18	21	71
1 % rose bengal combined with 1 % fluorescein	81	65	73	49
Total	23	23	23	460

fluorescein combined with 1 % rose bengal as many as 35 per cent of this group had more than 1000 dots scattered over the cornea (table III).

The minute dots rose in number with increasing years. The subjects under 40 presented maximally 9 dots, while up to 100 dots or more could be seen after the age of 60 after instillation of 0.125 % fluorescein (fig. 1).

A similar rise was seen after instillation of a *mixture* of 1 % rose bengal fluorescein with maximum 9 dots before the age of 30, against up to 100 000 diffusely over the cornea after the age of 50.

Material

The total material examined comprised 460 normal eyes and 192 pathological from 326 subjects The diagnoses in the pathological cases are shown in table IV

Results

Micropunctate fluorescein staining was most frequently seen after instillation of 1 % fluorescein combined with 1 % rose bengal

There seemed on the other hand to be no difference between the eyes treated with 0 125 % fluorescein alone and those also given oxibuprocaine (no vesin) and a preservative The two latter groups have therefore been dealt with collectively in the paper

Normals

Incidence of Micropunctate Staining

One normal out of every six showed micropunctate staining of the cornea after instillation of 0 125 % fluorescein The number having stainable corneae was seen to rise with increasing years Micropunctate staining was observed in no more than 4 % of normals under 40 years of age against in 20 per cent over 50 The incidence seemed to rise steadily until the age of 50 and then to remain unchanged

Micropunctate fluorescein staining was even more frequent after instillation of 1 % fluorescein combined with 1 % rose bengal This gave staining in 73 per cent of the normals examined The frequency of stained corneae followed approximately the same age curve as that after the weaker fluorescein (table I)

No unquestionable sex difference was detectable The possible female preponderance after staining with rose bengal and fluorescein (table II) was not statistically significant The larger fluorescein oxibuprocaine stained series showed no sex difference

Number of Minute Dots

After instillation of 0 125 % fluorescein minute dots were seen in 17 per cent of the normals In most cases the number of such dots was very small and only recognizable by the technique described above No more than 1 per cent displayed over 100 dots (table III)

The number of dots seen was considerably greater after instillation of 1 %



Fig 1

Micropunctate fluorescein staining of normal corneae Dependence on age 411 eyes stained with 0 125 % fluorescein Abscissa patient s age Ordinate Percentage number of eyes stained The hatching and colouring of the columns indicate the number of minute dots per cornea

In the presence of many dots the counting was based on an estimate The dots within a corneal area exposed to light through a suitably small slit were counted The total number was thereafter calculated from this value Maximum was 10^3 in normal cases and perhaps 10^6 in pathological In the latter the cornea was spotted with almost confluent fine dots

Pathological Cases

This report does not include true fluorescein staining where a fairly large area is distinctly stained as seen for instance in cases of erosion Fluorescein staining could be expected in only few cases of the present series (table IV)

Nevertheless micropunctate fluorescein staining was more frequent and more extensive than in normals

Such staining with roughly up to 10^5 minute dots was frequent in cases of conjunctivitis sicca corrosion and foreing bodies on the cornea and also relatively frequent in keratitis corneal dystrophy and corneal opacity

Minute dots were also more frequent in the presence of such diseases as are

Table III

Micropunctate fluorescein staining in a series of normal eyes and in a pathological material after instillation of *0 125 % fluorescein or 1 %* fluorescein combined with 1 % rose bengal

dye	clinical condition	*Punctate fluorescein staining percentage number of corneae*							
		none*	1–4*	5–9*	10–24*	25–99*	100–999*	≧ 1000*	number of eyes
0 125 % fluorescein	normal	83	9	4	3	1/2	1	0	411
0 125 % fluorescein	pathol	41	10	6	18	10	8	8	125
1 % flu rose bengal	normal	27	16	2	4	0	16	35	49
1 % flu rose bengal	pathol	18	12	3	22	4	19	21	67

* Number stated of minute dots per cornea

In the presence of many minute dots these were as a rule evenly scattered over the whole cornea Few dots on the other hand were accumulated within a certain limited area most often inferiorly close to the limbus or nasally at the limbus or below and nasally at the corneal limbus (fig 2)

The dots were diffusely present in 20 per cent of all who displayed micro punctate fluorescein staining

In 62 per cent the dots were situated inferiorly nasally or in between

The dots were rarely found grouped temporally superiorly or centrally on the cornea (table V)

The sites of the dots were independent of the dye solution used and also seemed to be independent of the diagnostic group

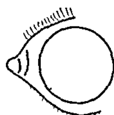


Fig 2

Example of typical localized micropunctate fluorescein staining of the cornea

Table V

Sites of micropunctate fluorescein staining on the cornea (normal and pathological cases) percentage distribution.

diffusely	20
nasally	10
inferiorly	39
below and nasally	13
temporally	[illegible]
centrally	5
superiorly	5
mixed	5

Table IV
Pathological material examined for micropunctate fluorescein staining of the cornea.
Number of corneae examined

	fluorescein 0 125 %	comb 1 % fluorescein and 1 % rose bengal
contact lens wearers	6	12
keratitis	4	16
keratoconjunctivitis sicca	4	2
corneal dystrophy	3	2
corrosion foreign body	7	7
corneal opacity	8	0
chron simple conjunctivitis	26	14
infectious conjunctivitis	7	5
glaucoma	38	1
other	22	8
Total	125	67

Other comprise aphakia pterygium papillomatous conjunctivitis chemosis exophthalmos chalazion phthisis facial nerve palsy iritis

not supposed to involve the cornea than in normal eyes though with a fairly small number on the individual cornea e g in chronic simple conjunctivitis

Eyes with infectious bacterial conjunctivitis showed similar conditions as normal eyes

Contact Lens Wearers

Six had 0 125 % fluorescein instilled In one no micropunctate staining was seen and in one more than 1000 dots while the remaining showed between 5 and 100 dots (Ages 19 57 average 35)

Twelve had a 1 % rose bengal fluorescein mixture instilled They all presented minute dots three less than 25 dots and five more than 1000 one of the latter as many as about 10^5 (Ages 18 58 average 36)

Rubbing

Intense rubbing on closed lid may provoke micropunctate fluorescein staining In some instances up to 30 dots could be elicited while in others no such were visible even after repeated rubbing

Such defects were most frequent among the elderly subjects suggesting that the corneal epithelium becomes increasingly vulnerable in the course of years

In a previous study (*Norn* 1969) I noticed that the precorneal film bursts sooned in women than in men (wetting time on an average shorter in women than in men)

This poorer protection of the female cornea might be conceived to result in a more frequent occurrence of micropunctate fluorescein staining among wo men In the series under review no significant difference was demonstrated however

Gronvall as early as 1937 showed that the absorption through the cornea is greatly promoted by corneal defects Presence of minute fluorescein stainable defects possibly renders the corneal epithelium barrier less resistant so that ac cordingly locally applied substances are much more readily absorbed in normal eyes with such defects than in other normal eyes having no defects

The results of the present investigation suggest that a minor proportion of the microdefects are within the physiological range and that these occur particu larly in elderly individuals

The phenomenon makes it difficult to distinguish between definitely patho logical punctate fluorescein staining and physiological micropunctate staining

The smaller the number of minute fluorescein dots the older the patients and the higher the fluorescein concentration used the greater is the probability that the staining may be regarded as being within the physiological range

If on the other hand *many minute dots are seen especially in a fairly young individual the finding is to be characteri ed as pathological* (After instillation *of* 0 1°5 % fluorescein over 100 dots were seen in no normal individual under 60)

In a contact lens wearer micropunctate fluorescein staining *must* be *claimed* in practice to be a sign of interrupted continuity of the cornea a *defect which* may constitute the point of entrance of infection *The staining is therefore a danger signal*

Unfortunately *normal cornea exist having a small number of such defects* These defects will naturally persist when contact lenses are worn

On noticing micropunctate fluorescein staining in contact lens wearers a cause of this must be searched for If the stainability cannot be eliminated by changing contact lens insertion technique or wearing time the phenomenon may be no more than a physiological microstaining

As however it is impossible to decide whether this is so the patient will have to remain under control

Rose Bengal Staining

Rose bengal stains degenerated epithelial cells and mucus

Fluorescein stains epithelial lesions the interrupted continuity allowing the dye solution to penetrate and diffuse among the epithelial cells sometimes right into the aqueous humour Hence some areas are only stained by rose bengal and others only by fluorescein (*Norn* 1964 B)

Accordingly the present material presented areas stained by rose bengal alone but with absolutely no fluorescein stained dots in this areas

Conversely in a case of slaked lime corrosion no rose bengal staining nor true fluorescein staining was observed 48 hours after the corrosion whereas numerous minute fluorescein dots were seen at a site corresponding exactly to the corroded area and limited to this

In rare cases only did rose bengal staining and micropunctate fluorescein staining occur within the same area

The site of the minute dots bore no relation to Hudson Stähli s line

Discussion

Similarly as ordinary fluorescein staining is due to interrupted continuity of the cornea micropunctate staining is supposed to be due to a defect of the corneal surface

Fluorescein diffuses rapidly from the micro lesion to the surrounding part of the cornea thereby rendering an estimation of the size of the defect impossible

The dots are so minute that they must be supposed to be due either to dropping out of a single cell or to a defect between two epithelial cells which allows dye to penetrate into the intercellular space

The present investigation showed that such defects by no means are rare even among normals but that they often are only detectable by use of an accurate and careful technique

The defects were visible in the greatest number after staining with a 1 % rose bengal fluorescein mixture This was due to the higher fluorescein concentration in this solution and perhaps also to the fact that simultaneous instillation of rose bengal may cause irritation and possibly provoke hole formation

On the other hand defects were also found in normals after instillation of 0 125 % fluorescein to which no other substances had been added and which caused no irritation

Addition of oxibuprocaine (novesin) or a preservative (0 0025 % phenylmercuric nitrate) did not raise the number of minute dots

Such defects were most frequent among the elderly subjects suggesting that the corneal epithelium becomes increasingly vulnerable in the course of years

In a previous study (*Norn* 1969) I noticed that the precorneal film bursts sooned in women than in men (wetting time on an average shorter in women than in men)

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The results of the present investigation suggest that a minor proportion of the microdefects are within the physiological range and that these occur particu larly in elderly individuals

The phenomenon makes it difficult to distinguish between definitely patho logical punctate fluorescein staining and physiological micropunctate staining

The smaller the number of minute fluorescein dots the older the *patients* and the higher the fluorescein concentration used the greater is the probability that the staining may be regarded as being within the physiological range

If on the other hand *many minute dots are seen especially in a fairly young individual the finding is to be characterized as pathological* (After instillation of 0 125 % fluorescein over 100 dots were seen in no normal individual under 60)

In a contact lens wearer micropunctate fluorescein staining must be claimed in practice to be a sign of interrupted continuity of the cornea a defect which may constitute the point of entrance of infection *The staining is therefore a danger signal*

Unfortunately *normal cornea exist having a small number of such defects* These defects will naturally persist when contact lenses are worn

On noticing micropunctate fluorescein staining in contact lens wearers a cause of this must be searched for If the stainability cannot be eliminated by changing contact lens insertion technique or wearing time the phenomenon may be no more than a physiological microstaining

As however it is impossible to decide whether this is so the patient will have to remain under control

Summary

Microdefects of the surface of the corneal epithelium were detected after staining with 0 125 % fluorescein in 17 per cent out of 411 normal eyes and after staining with 1 % fluorescein combined with 1 % rose bengal in 73 per cent out of 49 normal eyes

After instillation of 0 125 % fluorescein only few dots were counted (over 100 in 1 per cent of all the normal eyes) After combined fluorescein and rose bengal on the other hand more than 1000 dots were found in 35 per cent

The incidence of micropunctate staining and the number of dots were seen to rise with increasing years

Among the pathological cases micropunctate staining was more frequent and the number of dots greater particularly so in the presence of corneal lesions but also in other cases e g chronic simple conjunctivitis

The point of transition from physiological punctate staining to pathological fluorescein staining is indefinite and renders assessment difficult e g in the cases of contact lens wearers Micropunctate fluorescein staining is however always a danger signal

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GLAUCOMA AND RIEGER S SYNDROME

BY

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Most cases of iridocorneal dysgenesis suffer from glaucoma or eventually develop high intraocular tension (*Rieger* 1935 *Braendstrup* 1948 *Kittel* 1956 *Busch et al* 1960 *Frandsen* 1963) In the numerous reports already available the elevated intraocular pressure has ben ascribed to an obstruction of the filtering angle by abnormal tissue of mesenchymal origin A report is made of 2 patients one with a typical syndrome and glaucoma and the other whose glaucoma was mainly due to an angle closure mechanism

Case 1

In August 1968 a young recruit aged 19 /2 years was referred to the eye clinic because of ocular pain and headaches after reading The left eye was weak since birth when it appeared to have an *eccentric* pupil Two years before the patient had an abdominal operation due to diverticulitis of the *small intestine* The parents and younger brother were normal Visual acuity was 6 6 in the right eye with a -1 50 sph correction and 6 30 in the left eye The *cor eas* measured 9 mm vertically and 10 0 mm horizontally Applanation tonometry gave *readings of* 34 mm Hg in the right and of 3? mm Hg in the left eye Both anterior chambers were of normal depth In the right eye the anterior leaf of the iris *was extremely* atrophic and the pupillary sphincter stood out like a ring The pupil was pointed *temporally* and reacted sluggishly to light There were several broad bridges of iris *tissue* attaching to the periphery of the cornea which showed a thickening in the periphery of Descemet s membrane (Fig 1 RE) Gonioscopy demonstrated a slightly *protruding* Schwalbe line the already described abnormal iris attachments which also *were connected* in some areas to the root of the

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Fig 1

Right eye of male aged 19/₂[1] with atrophy of the anterior leaf of the iris displaced posterior embryotoxon and broad adhesions between the iris stroma and the peripheral cornea

Left eye *of same patient – iris atrophy The pupil is drawn and temporally* Note broad adhesions between the iris stroma and the peripheral cornea

trabecular meshwork and an abnormal greyish opaque tissue covering the angle of the anterior chamber which was open and of intermediate depth

In the left eye the iris was also atrophic The pupil was drawn down and temporally and bridges of abnormal tissue connected the periphery of the iris to the Schwalbe line and to the peripheral cornea from 2 to 7 o clock (Fig 1 LE) Gonioscopy showed an open angle of intermediate depth A prominent Schwalbe line was present The angle was covered by an avascular structure of characteristics similar to the right eye The broad iridocorneal adhesions were seen at 2 30 to attach also to the root of the trabecule

The media and fundi were normal except for superior and inferior crescents adjacent to the discs The right visual field was normal and the left could not be charted

On the basis of the malformation involving the angle of the anterior chamber iris stroma and peripheral cornea including abnormal strands of iris attaching to the trabecule and *in the periphery of the cornea to* a posterior embryotoxon *the diagnosis* was made of a dysgenesis mesodermalis cornea et iridis or Rieger s syndrome

Treatment consisting of 2 % pilocarpin drops d s and Eppy 1 % b d in both eyes succeeded in controlling the intraocular pressure An optic iridectomy was performed in the upper temporal quadrant of the left eye This improved the visual aquity to 6/ 5

Case 2

A 47 year old male was referred to the eye clinic because of iridocorneal dysgenesis and elevated *intraocular pressure in both eyes The main clinical symptoms were frontal* headaches and transient attacks of ocular pain and redness accompanied by blurred vision especially in the left eye for the last 6 months

The examination revealed a visual aquity of 6/6 in each eye The right cornea measured 10 0 mm × 10 0 mm and the left 9 5 mm × 9 5 mm A marked posterior embryotoxon was present in both sides Atrophy of the iris stroma was present bilaterally Broad iridocorneal adhesions were seen peripherally in both eyes In the right eye there was in addition a tangential band of iris tissue extending from 2 30 to 6 30 and attaching to the cornea in its center (Fig 2) The pupils were pointed downwards

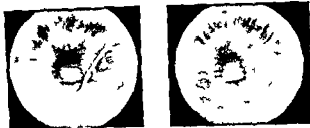


Fig 9

Right eye of male aged 49 Note atrophy of anterior leaf of iris broad adhesions between iris and displaced posterior embryotoxon and fibrous iris and from 2 30 to 6 30 adhering in its central part of the cornea

Left eye of same patient Similar iris atrophy and broad adhesions between iris and peripheral cornea

and reacted very poorly to light in both sides Applanation tonometry revealed tensions of 40 mm Hg in the right and of 50 mm Hg in the left eye After a mydriatic instillation the tension rose by 10 mm in each eye Both anterior chambers were very shallow

The lenses presented pinpoint opacities The vitreous and fundi were normal Visual fields were not impaired

Gonioscopy performed when the intraocular pressure was high revealed almost completely closed angles in both eyes Only a small nasal and lower segment could be seen of each angle up to the scleral spur After 2 % pilocarpin drops the pressure dropped to ?2 mm in the ri ht and to 20 mm in the left eye Repeated gonioscopy under the miotic influence revealed open angles up to the scleral spur In both angle recesses there was a brownish cob web like structure with whitish dots A few irido corneal adhesions were seen attaching to the scleral spur

Treatment consisted of peripheral iridectomies in each eye to treat the closure angle component in this case of iridocorneal dysgenesis After surgery the tension was regulated with pilocarpin 2 % twice daily

Discussion

Rieger s *syndrome is a mesodermal* developmental abnormality consisting of iris hypoplasia especially of the anterior layers and abnormalities in the angle of the anterior chamber produced by a more or less marked abnormal *tissue* and by strands of iris adhering to a posterior corneal embrytoxon Associated with the syndrome different systemic abnormalities due to ectodermal mal development have been reported (*Hagedoorn* 1937 *Henkes* 1965) Most of the affected patients have *or will eventually* develop glaucoma The elevated intra ocular pressure has always been linked to the abnormal tissue blanketing the

filtering angle, the more severe the angle dysgenesis causing the more severe glaucoma although glaucoma is known to be present also in milder forms of Rieger s syndrome (*Pearce* and *Kerr* 1965) Although the malformation is con genital glaucoma usually develops later in life in distinction to congenital glaucoma or buphthalmos

Case 1 in this report represents a typical case in which the abnormal tissue in the angle has produced a juvenile glaucoma

In Case 2 a middle aged patient the glaucoma was of different charac teristics The angle of the anterior chamber in this patient, was not obstructed by an obvious abnormal tissue It was mainly an angle closure mechanism which caused the elevated pressure This was demonstrated gonioscopically by ex amining the angle under elevated and normal tension Although the mechanism of this angle closure is not clear, it seems possible that the extensive adhesions bridging the root of the iris to the periphery of the cornea in both eyes could have pulled the iris forward causing shallow anterior chambers Such a me chanism has also been postulated by Reese and Ellsworth The moderately mydriatic pupils whose motility was defective might have caused a relative pupillary block These 2 components could well have played an important role in the mechanism of glaucoma Peripheral iridectomies eliminated the closure angle component of the glaucoma probably by interfering with the pupillary block component

Summary

A report is made of 2 patients affected with iridocorneal dysgenesis (Rieger s syndrome)

Case 1 was a typical case in which the juvenile glaucoma was due to blanket ing of the filtering angle by abnormal mesodermal tissue

In Case 2 no obvious abnormal tissue obstructed the filtering angle Glau coma developed in middle age mainly due to a closure angle mechanism It is probable that the closure of the angle was produced by the iridocorneal adhe sions pulling forward the iris and by a pupillary block component due to re lative midriasis and poor pupillary motility

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present one might be due to fresh mutations or more probably to the well known variation in penetrance of the particular gene The reasons for this variation in penetrance are not known but genotypic factors such as suppressive or otherwise interacting genes as well as promoting or suppressing environmental factors are to be considered

The strong hereditary influence on the tumour development has motivated cytogenetical analysis of cultured normal fibroblasts or/and leukocytes from patients with retinoblastomas and sometimes also of their relatives (4 7) No karyotypic deviations from normal have been found in these instances except in one case (4) This patient a 10 month old girl belonged to the category of sporadic cases and chromosomal analysis disclosed a deletion of the long arm of one of the D group chromosomes probably a no 15 This aberration was found in all cells analyzed from cultures of conjunctival and dermal tissue blood cells as well as tumour tissue In explants of tumour tissue there was in addition an unusually high number of cells with chromosome numbers of 40 or less but with no consistent pattern No exact counts or karyotypes were given nor any information about the duration of the cultures

To my knowledge this is the only cytogenetical analysis of a retinoblastoma and it should be observed that the chromosomes were studied only in tissue culture explants To avoid the potential risks of chromosomal changes during culture direct fixations from the tumour were primarily used in the present analysis First aim of the present study was to look for whether the deleted D chromosome of Lele et al (4) would be found Second the chromosomal picture was analyzed in relation to the remarkable hypodiploid pattern reported by Lele et al Third the findings were compared with those obtained from chromosomal studies of some histologically related tumours

Material and Methods

The present sporadic case concerned a girl 1 year and 10 months at the time of operation. Strabismus and a greyish right pupil had been noticed for at least 4 months prior to operation. The right eye was found to contain a tumour Macroscopic examination of the enucleated eye revealed a bulging yellow white tumour which had replaced the corpus vitreum The histological picture was that of a poorly differentiated retinoblastoma (Fig 1a) which only in small areas showed a tendency towards rosette formation (Fig 1b) Mitotic figures were numerous and some of the anaphases were abnormal with lagging chromosomes and/or multipolarity There was no scleral infiltration or extension along the optic nerve

For chromosome preparation small pieces of the soft tumour tissue were finely minced withwith scissors suspended in Parker s medium 199 and incubated at 37° C for 2 4 and 8 hours respectively Colcemid (CIBA) was added to a final concentration of 1 μg/ml for the suspensions harvested after 2 and 4 hours and to a concentration of 0 2 μg/ml

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CHROMOSOMAL ANALYSIS OF A HUMAN RETINOBLASTOMA

BY

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Summary

The chromosomes of a sporadic human retinoblastoma were studied in fixations directly from the tumour The karyological picture was characterized by the following features hyperdiploid stem sidelines with characteristic marker chromosomes a restricted spread around the stemline number and some polyploid mitoses The findings differred completely from the inconsistent pattern reported for another sporadic retinoblastoma investigated exclusively after explantation *in vitro* In this previously described retinoblastoma a deletion affecting one of the long acrocentrics was found both in normal and tumour cells This deletion was not seen in the present case

A comparison was made with chromosome conditions reported from medullo and neuroblastomas without finding any obvious similarities

In vitro investigations of the present retinoblastoma indicated an early and gradual substitution of the tumour cells by stroma cells

Introduction

The development of human retinoblastomas is believed to be dependent on the presence of a single dominant gene The occurrence of sporadic cases as the

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for that taken after 8 hours Hypotonic treatment was performed by adding 3 parts distilled water to 1 part suspension After 20 minutes the suspension was centrifuged the supernatant discarded and 60 per cent acetic acid 0 1 N hydrocloric acid fixative added for 30 minutes The pellet was then stained in 2 per cent orcein and squashes made on siliconized slides All counts of metaphase were repeated 2 or more times Karyotype analyses were made by photography

Pieces of tumour tissue were also explanted *in vitro* using milk dilution bottles and Parker's medium 199 supplemented with 10 per cent unfiltered inactivated calf serum Chromosomal preparation was performed as described above except for a somewhat weaker hypotonic treatment

Results

1 Numerical Findings

The chromosomal findings in the three consecutive fixations directly from the tumour showed no differences and the results were pooled in Table I As seen from this table there was a sharp mode at 47 the stemline (S) number The spread around the S number was moderate and *restricted to S ± 3 but the distri*

Table I

Chromosome number distribution a sharp mode at 47

Chromosome numbers																		Total
44	45	46	47	48	49	50	51	78	84	85	86	87	88	89	90	91	92	
	16	9	108	93	5	1	1	1	2	–	1	–	1	–	2	–	1	173

Fig 1

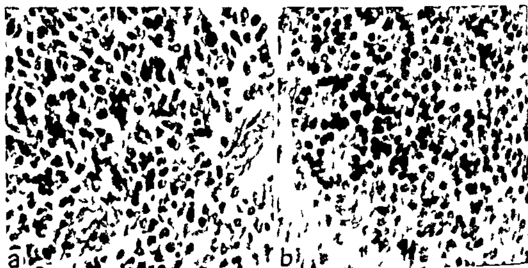
a Histological picture of the main part of the retinoblastoma No organoid structures Haematoxylin eosin × 330

b Small area with rosette like structures adjacent to one with reactive gliosis Haematoxylin eosin × 330

c Metaphase of the stemline S = 47 The arrow points at the small m_1 marker × 1035

d Metaphase of subgroup III 46 chromosomes The arrow points at the big m_2-marker 103

e Part of metaphase of subgroup II The big arrow points at the t_1 marker and in addition small arrows point at 8 double minutes × 4150



c

d

e

Fig 1

Table II

Kary types of 0 cells presented as *leviation from* normal female diploid or tetraploid karyotype Division into three subgroups on the basis f marker distribution (last columns)

Number f chr mosomes	Number of cells	Chromosome grou[s 1		3	4	C \ 12	13–15	16	17–18	19–20	21–2	Markers t_1	t	m_1	m	Subgroup I III
45	1	+1	–	–	+1	–1	–	–	–	–	–1	–	–	+1	–	
45	9	+1	–	–	+1	–?	–	–	–1	–	–1	–	–	+1	–	
46	1	+1	–	–	+1	–	–	–	–	–	–1	–	–	+1	–	
41	1	+1	–	–	+1	–1	–	–	–1	–	–1	–	–	+1	–	
47	4	+1	–	–	+1	–	–	–	–1	–	–1	–	–	+1	–	
47	19	+1	–	–	+1	–1	–	–	–	–	–1	–	–	+1	–	I
48	7	+1	–	–	+1	–	–	–	–	–	–1	–	–	+1	–	
43	1	+1	–	–	+1	+1	–	–	–	–	–1	–	–	+1	–	
56	1		–	–	+?	–9	–	–	–	–	–1	–	–	+1	–	
90	1	+?	–	–	+?	–6	–	–	–	–	–2	–	–	+2	–	
9?	1	+?		–	+?	–C	+2	–	–	–	–?	–	–	+2	–	
45	1	+1	–	–	+1	–9	–1	–	–	–	–1	+1	*	+1	–	
45	1	+1	–	–	+1	–?	–1	–	–	–	–?	+1	–	+1	–	
46	1	+1	–	–	+1	–1	–1	–	–	–	–2	+1	–	+1	–	II
4C	1	–	–		+1	–?	–	–	–1	–	–1	+1	+1	+1	–	
43	1	–	–	–	+1	+?	–1	–	–	–	–1	+1	–	+1	–	
49	1	+1	–	–	+1	–	–	–	–	–	–1	+1	–	+1	–	
45	1	–1	–1	–	+1	+1	–1	–	–1	–	–	–	–	–	+1	
45	?	–1	–	–	–	+1	–1	–	–1	–	–	–	–	–	+1	III
47	1	–?	–	–	+1	+2	–	–	–1	–	–	–	–	–	+1	
54	1	–1	–	–	+?	–6	–?	–	–	–	–2	–	–	–	+1	

Double minutes excluded

bution was asymmetrical due to excess of 48 chromosome cells About 5 per cent of the counted cells were polyploid Since it was possible to make exact counts in almost every metaphase detected during the screening and the incidence of evidently broken cells was low the recorded frequency of polyploids can be regarded as a good estimate of the true frequency Numerically it was noteworthy that none of the polyploid cells represented a simple doubling product of the stemline

II Markers

Fifty one metaphases were subjected to detailed karyotype analysis most cells had the S number but several diploid near diploid and some polyploid variant cells were included In Table II the karyotyped cells were divided into 3 subgroups according to the distribution of 3 different markers About 78 per cent of the cells analyzed belonged to subgroup I characterized by the occurrence of one or in the tetraploids two metacentric markers (m type according to the nomenclature proposed by Levan et al (5)) This m_1 marker was intermediate in size between pair no 16 and the biggest pair of nos 19 20 (Fig 1c 2 3a and b) Subgroup II encompassed about 12 per cent of all metaphases analyzed in addition to the m_1 marker described above all cells showed an acrocentric marker (t type) At the same time one nos 13 15 was missing in 4 of the 6 cells analyzed This t_1 marker was almost twice as long as the longest pair in the group nos 13 15 and it had a vague secondary constriction in the middle of the long arm (Fig s 1e 3a and b) Subgroup III with about 10 per cent of the cells had no m_1 or t_1 marker but a big metacentric marker (m type) here one no 1 was missing in all cells The m_2 marker was similar to pair no 9 with regard to arm index but both arms were about 25 per cent longer than those of pair no 2 (Figs 1d 3c) The three described markers m_1 t_1 and m had the same morphological appearence and relative size in different cells within each of the subgroups

Other types of markers were seen only in two cells both belonging to the second subgroup (Table II) In one 46 chromosome cell there was a small acrocentric marker t half as big as the smallest pair of the G group (Fig 3b) The other cell had 45 chromosomes including the m_1 and t_1 markers and in addition 8 or possibly 9 minute chromatin bodies (Fig 1e) The size of some of them was at the border of visibility which accounted for their reduced stainability They clearly had two chromatids which often were more separated than in ordinary chromosomes At least some of the minutes seemed to be centric In all their characteristics they agreed with the double minutes in some Rous mouse sarcomas (8) and they will be termed double minutes here too

The two cells with deviating marker sets did not influence the general picture of the distribution of m_1 t_1 and m markers The impression that the

bution was asymmetrical due to excess of 48 chromosome cells About 5 per cent of the counted cells were polyploid Since it was possible to make exact counts in almost every metaphase detected during the screening and the incidence of evidently broken cells was low the recorded frequency of polyploids can be regarded as a good estimate of the true frequency Numerically it was noteworthy that none of the polyploid cells represented a simple doubling product of the stemline

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a

m1

b

m1

c

m1

d

m1

Fig. 6

Karyotypes of a and b the stemline S = 47 one m_1 marker c the sideline s_1 = 48 one m_1 marker and d the sideline s = 47 one m_1 marker The chromosomes grouped according to the Denver classification × 2190

tumour cell population was composed of three different subgroups of cells was further strengthened by the numerical variation within each group

III Karyotypes of Stem Sidelines and Variant Cells

Twenty three of the 24 analyzed cells with 47 chromosomes belonged to sub group I and 19 of them had identical karyotype In addition to the m_1 marker this karyotype was characterized by an extra of each no 1 and nos 4 5 and a loss of one nos 6 X-12 and one nos 21 22 (Figs 1c 2a and b) These cells constituted the stemline Since the 47 chromosome cells were random samples, it can be calculated that almost 50 per cent (49 4 per cent) of the counted tumour cells belonged to the stemline (Tables I and II) The other four 47 chromosome cells of subgroup I all differred from the stemline by loss of one nos 17-18 instead of one nos 6 X 12 (Fig 2c) A similar calculation of the incidence in the tumour cell population of this particular karyotype gave a frequency of about 10 per cent (10 4 per cent) These cells were regarded as a sideline (s) according to the nomenclature adopted in previous investigations (*e g* 8) a minimum of 10 per cent of a certain karyotype was required for this designation A second somewhat more prominent sideline was found in sub group I having 48 chromosomes and differring from the S by having the normal number of 6 X 12 chromosomes (Fig 2d) All 48 chromosome cells analyzed belonged to this sideline which had an estimated frequency in the tumour cell population of about 13 per cent (13 3 per cent)

The rest of the diploid near diploid cells of subgroup I were evidently variant cells closely related to the stem sidelines though their exact mode of origin could not be determined The same was probably true of the few tetraploid cells but most of them seemed to have undergone secondary changes after the doubling of the chromosome number

No definite sidelines could be identified in the other two subgroups II and III However the cells within each group showed great similarities both in numerical and structural variation Thus it might be justified to regard each of the small subgroups as a counterpart to a sideline probably having similar importance in the population dynamics The karyological findings in both sub group II and III indicated that they were derived from subgroup I

Though the origin of the m_1 marker could not be traced with certainty the situation was somewhat different for the t_1 and m markers Thus as pointed out in a previous section the t_1 marker appeared at the same time as one nos 13 15 was lost in 4 of 6 karyotyped cells It seemed reasonable to assume that the t_1 marker represented a remodelled long acrocentric Analogously the m marker might well be derived from a chromosome no 1 one or two chromosomes no 1 were missing in all cells of subgroup III

The frequency of breakage was only about 5 per cent in all fixations and

none of the markers were ever affected Thus it is resonable to assume that the markers were formed early in tumour development creating conditions for a fairly long period of stabilization of the newly formed chromosomes The morphological constancy and lack of any appreciable variation in size at the time of fixation were characteristics of the markers supporting this assumption

IV In Vitro Results

The development of the material explanted *in vitro* was followed continously in the inverted microscope During the first week the cells attached to the wall consisted of small uniform element arranged into loose sheets These cells ra pidly degenerated during the following week and the few cells left were larger and spindle shaped They grew very slowly and it was not possible until 70 days after explanation to make fixations for chromosomal analysis At that time the cells formed sheets but contact inhibition was preserved

Only one fixation was successful and among the 30 countable metaphases 22 had 46 chromosomes and 8 had 92 chromosomes All karyotypes were nor mal female diploid or tetraploid Thus both cell morphology and chromosomal analysis indicated that the finally outgrowing elements represented stroma cells It could not be decided whether the comparatively high frequency of tetraploid cells was a characteristic of the stroma cells explanted or a response to the *in vitro* conditions

Discussion

The present retinoblastoma differred in chromosomal picture from the retino blastoma reported by Lele et al (4) Instead of an inconsistent hypodiploid pattern the present case was characterized by a well defined hyperdiploid stem line and two small sidelines both closely related to the stemline About 3/4 of the tumour cell population belonged to the stem sidelines and the variant cells showed a pattern of karyotypic deviations deducible from the stemline

No deletion of a D chromosome was noticed in the present case either in the tumour cells or in the normal cells growing in the tissue culture Thus the pre sent case does not support the thought of Lele et al (4) that sporadic retino blastomas may develop as a consequence of the hemizygous condition of a D chromosome segment specifically involved in the formation of these tumours Thus the localization of the gene for development of retinoblastomas remains uncertain Investigations of further cases might elucidate this question as also the possible genic control of the karyotypic evolution in the retinoblastomas

Histologically the retinoblastomas are very similar to two other types of neu

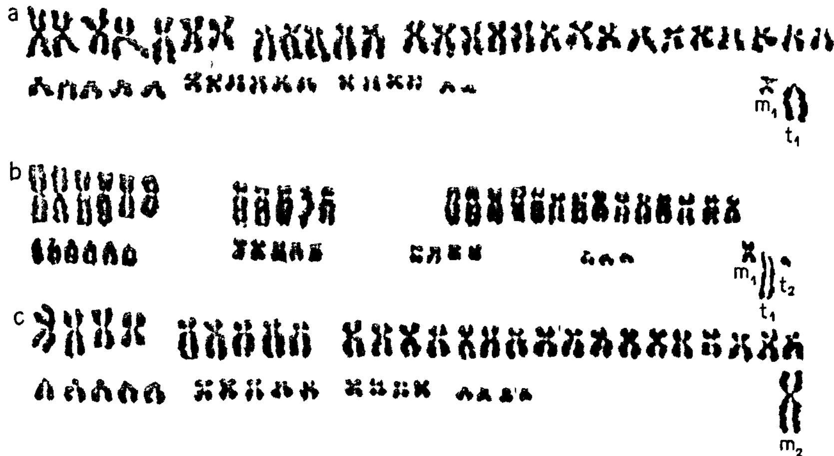


Fig 3

Karyotypes of variant cells from a subgroup II 46 chromosomes one m_1 marker and one t_1 marker b subgroup II 46 chromosomes one m_1 one t_1 and one t marker and c subgroup III 45 chromosomes one m marker × 2190

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Histologically the retinoblastomas are very similar to two other types of neu

rogenic tumours the medulloblastomas and the neuroblastomas Comparatively few of each type have been studied chromosomally (1 3 6 13 and references in 8) and among those reported there is a variety of cases with a seemingly normal diploid stemline and also with an abnormal either diploid near diploid or polyploid stemline None of them shows any clear karyotypic similarities to the present case However some of them belong to the restricted category of human tumours showing the structural aberration termed double minutes As pointed out earlier one of the studied 173 cells of the present retinoblastoma showed this aberration Since the phenomenon has been observed in one or a few cells of several astrocytic gliomas (2 11) and some gastrointestinal carcinomas (12) it might be that this aberration is more common than apparent from the reports though it is still believed that an engagement of a major part of a tumour cell population is definitely a rare event

Recent studies of human and animal tumours have demonstrated a correlation between pathological parameters and chromsomal findings (for review see (10)) Consequently it is interesting to note that the considerable karyotypic remodelling in the present retinoblastoma was parallelled by a poorly differentiated histological character The formation of rosettes is regarded as a characteristic of more mature tumour types with a less severe prognosis Further cases will reveal if these more mature types have a correspondingly more normal chromosomal picture

The inability to establish a tumour cell culture during prevailing *in vitro* conditions is apparent The stromal replacement which already seemed to start during the second week was a phenomenon in line with findings in Rous virus induced sarcomas of the mouse (9) In view of the uncertainty as to what cells grow out in tissue culture it is definitely safer to make the chromosomal analyses on direct fixations from the tumour whenever possible As a rule only fixations from real short term cultures (3) may be regarded as a reliable substitute or complement to the direct fixations

Acknowledgements

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Department of Physiology Karolinska Institutet Stockholm

THE ERG AND OPHTHALMOLOGICAL CHANGES IN EXPERIMENTAL METALLOSIS IN THE RABBIT

I Effects of iron particles

BY

BENGT KNAVE

Introduction

Retained intraocular iron particles can give rise to changes in the different tissues of the eye called *siderosis bulbi* Retinal damage often occurs at an early stage and is the most detrimental result of siderosis

After introducing electroretinography (ERG) for clinical purposes *Karpe* (1948 1957) showed that pathological changes in the ERG could be correlated to retinal siderosis which finding has been confirmed in other clinical investigations (*Schmoger* 1956 *Straub* 1961 *Kozousek* 1965 *Knave* 1969a)

In the last mentioned of these investigations the most case material was presented 68 cases were selected for analysis 42 of which with an intraocular iron particle Localization duration and degree of encapsulation of the intraocular particles did not explain the differences in the development of siderosis from case to case The results indicated that minor differences in alloy content might play a role

The clinical results thus pointed to the necessity of an experimental approch in animals It should be mentioned that the ERG following intraocular im

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plantation of iron pieces has earlier been described in two studies on rabbits (Sugita et al 1960 Seto 1960) the results of which were ambiguous Sugita reported that the *b* wave following the implantation of an iron pin either decreased was constant or increased Seto on the other hand found a progressive decrease from day to day The *a* wave and the oscillatory potential were not evaluated ophthalmoscopical findings were not presented and the observation time was too short (one and two months respectively)

In the present investigation the changes in the *a* and *b* waves as well as in the oscillatory potential were studied during a long period (up to 1½ years) after implantation of pure iron particles in the vitreous of the rabbit The investigations were made with a recently described method which was used in studies on long term changes in retinal function induced by high intensity flashes (*Knave* 1969b) Moreover ophthalmological examinations were performed the results of which were compared with those of the electrophysiological investigations

Material and Methods

Electroretinogram The method which has been described in detail in a previous work (*Knave* 1969b) allowed repeated ERG recordings during a long period of time (in this study 1½ years) in the non anaesthetized rabbit. Due to strictly standardized experimental conditions the normal variations in the *b* wave were small Recordings were made simultaneously from both eyes which were illuminated with equal intensity one eye serving as test object and the other being used as reference The light stimulus consisted of an electronic flash (Braun F 87) the intensity of which could be varied by means of neutral filters In the present experiments the unattenuated flash intensity was used since high stimulus intensities are required to elicit an adequate *a* wave in the rabbit which has an F retina (*Granit* 1935) and to evoke an oscillatory potential (*Yonemura et al* 1963) The unattenuated flash had an intensity of about 7 log units above the *b* wave threshold of the dark adapted eye The average value of three recordings was used when evaluating the potentials When recording the *a* and *b* waves the first flash was applied to the dark adapted eye and the following flashes were presented with intervals of 10 min The oscillatory potential was obtained in response to flashes which were presented with intervals of 30 sec which provided a suitable photopic adaptation of the retina Different time constants were used in the recording system. When recording the *a* and *b* waves a time constant of 1 sec was used The time constant was 10 msec when recording the oscillatory potential Finally the *a* and *b* waves

were measured from their peaks to the isoelectric line The B-wave was defined as the total amplitude from the peak of the a-wave to the peak of the b wave.

In this connection mention must be made of the recently reported long term reversible changes in retinal function induced by short high intensity flashes (*Knave* 1969b c) In these studies it was found that even a single light flash with an intensity of about 7 log units above the b wave threshold of the dark adapted eye was followed by a slight but significant reduction of the b wave, obtained in response to a low intensity stimulus The reduction was found to last for about a week One hundred flashes with an intensity of about 9 log units above the b-wave threshold were shown to result in an initial increase followed by a transient decrease of the b-wave the recovery to pre illumination values being accomplished in about two weeks

As a consequence of these long term reversible flash effects the value of the test eye was always compared to that of the intact eye The normal variation of the relative differences between the right and left eye was investigated Table I shows these differences obtained on 8 rabbits (expressed in per cent of the higher value) Seven to 12 observations were performed in a period of 6 weeks In table I a plus sign (+) denotes that the right eye had the greater amplitude a minus sign (—) denotes the opposite condition Table I also shows the corresponding standard deviations for each animal On the basis of these data the weighted mean of the standard deviations for a single observation was calculated Thus the weighted $s_{a_{diff}} = 3\,9\,\%$ $s_{B_{diff}} = 5\,0\,\%$ $s_{b_{diff}} = 6\,8\,\%$ Although the latencies were not evaluated in detail it can be stated that their variation was in the same order of magnitude as that of the amplitudes

Table I

Normal variation of the differences between right and left eye ERG amplitudes obtained by a high intensity stimulus

Rabbit No	$\bar{a}_{diff}$ (%)	sa_{diff} (%)	$\bar{B}_{diff}$ (%)	sB_{diff} (%)	$\bar{b}_{diff}$ (%)	sb_{diff} (%)
1	— 2	5 2	— 1	4 1	— 1	5 1
2	+ 2	4 3	0	4 8	— 1	7 0
3	— 4	4 8	— 1	4 0	0	4 3
4	+ 1	2 9	+ 1	3 5	+ 1	5 6
5	— 1	3 9	— 2	4 3	— 3	4 8
6	+ 2	3 8	— 2	6 4	— 5	8 9
7	— 6	3 6	— 8	5 6	— 9	6 9
8	0	2 9	0	5 6	0	8 2

It should also be mentioned that the long lasting high intensity flash effects shown by Knave (1969b c) were of the same relative magnitude in eyes with varying degree of siderotic damage and in intact eyes

Ophthalmological examination The anterior segment of the eye was studied in a corneal *microscope* The posterior segment and the vitreous was examined by direct and indirect ophthalmoscopy The intraocular tension was grossly evaluated by means of careful palpation with small glass rods in no case there was any appreciable difference between right and left eye Moreover the corneal diameters were checked to be less than 15 16 mm to exclude eyes with glaucoma (*Kolker et al* 1966) Photographs of implanted particles were taken with an epitechnoscope camera (Zeiss)

Implantation technique The iron particles and in one experiment an iron salt solution were inserted (injected) transsclerally into the vitreous of the right eye Lumbar puncture needles (outer diameter 0 90 mm) were used for the scleral puncture when implanting the particles and a hypodermic needle (No 20 *outside diameter* 0 45 *mm) for the injection of* the solution The iron particles were loaded into the tip of the lumbar puncture needle ahead of the stylet and then sterilized by dry heat The needle was inserted just outside the corneal limbus (at about 6 o clock of its circumference) through the ciliary body and into the vitreous The solution was injected in the upper temporal quadrant of the bulb 7 8 mm from the corneal limbus All intraocular applications were performed in intravenous Narkotal® (Astra) or Nembutal® (Abbot) anaesthesia.

Implanted particles The implanted particles consisted of chemically pure iron (*purum* KEBO) Each particle had an area of 1 0 1 5 mm^2 *i e* the particles were small cubes with a side of 0 4 0 5 mm

Results

The electroretinogram following a scleral puncture

The electroretinographical changes following a scleral puncture with a lumbar needle are shown for two animals (A and B) in Fig 1 The results following a hypodermic needle puncture are shown for one animal in Fig 2 In the figures the puncture was performed at zero on horizontal time axis The ERG amplitudes (vertical axis) were expressed in per cent of those of the intact fellow eye The pre experimental relative amplitude values varied around 100 per cent from animal to animal In all the figures of the present study this variation was corrected for *i e* all the pre experimental values were adjusted to 100 per cent with subsequent correction of the following experimental values.

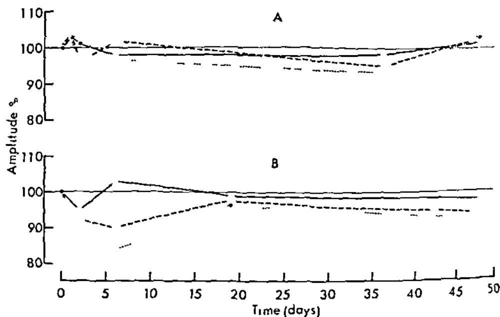


Fig 1
ERG amplitudes (in per cent of those of the intact fellow eye) following a lumbar needle scleral puncture (performed at zero on horizontal time axis) in two rabbits (A and B) Solid line represents the *a* wave dotted line the *b* wave and broken line the *B* wave the latter being defined as the total amplitude between the peak of the *a* wave and peak of the *b* wave

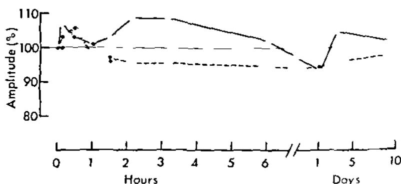


Fig 2
ERG amplitudes (in per cent of those of the intact fellow eye) following a scleral puncture (performed at zero on horizontal time axis) by a thin hypodermic needle Solid line represents the *a* wave dotted line the *b* wave and broken line the *B* wave the latter being defined as the total amplitude between the peak of the *a* wave and the peak of the *b* wave

in all the figures a solid line between filled circles represented the *a* wave a broken line the *B* wave and a dotted line the *b* wave

It is evident that a lumbar needle scleral puncture *per se* might induce a slight reversible reduction of the *B* and *b* waves during the first 1 2 weeks (Fig 1B) The *a* and *b* wave latencies and the oscillatory potential were not affected The hypodermic needle puncture was followed by *insignificant* amplitude changes As can be seen in Fig 2 an increase of the *a* wave and a reduction of the *B* and *b* waves were recorded a couple of hours after the puncture and two days later

On ophthalmological examination a slight leakage of vitreous was visible 3 5 hours following the scleral puncture performed with a lumbar puncture needle Moreover a slight flare in the anterior chamber was visible the first 4 5 days The scleral puncture by the thin hypodermic needle was not followed by any significant ophthalmological changes

Electroretinographical and ophthalmological changes following intravitreal application of iron particles

Iron particles were implanted in the vitreous of the right eyes of the rabbits as follows *one rabbit received 15 particles two rabbits received* 8 particles and two more received 4 particles The first mentioned of these animals was studied for more than three months the others for more than a year In an additional rabbit an iron salt solution was injected intravitreally

Implantation of 15 iron particles In Fig 3 the changes *in* ERG *after implantation* of 15 particles are presented Fig 3A illustrates the *a* *B* and *b* wave amplitudes (filled circles) and the scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye Fig 3B shows the peak latencies of the five first positive oscillations of the oscillatory potential *vi* o_1 *o* o_3 o_4 and *o* marked *with* triangles When affected these latencies always were found to increase compared to the normal latencies of the intact eye In the diagram this increase is expressed in msec

As can be seen in Fig 3A there was a fast initial decrease in the amplitudes After about 5 days this decrease was followed by a small increase and the amplitudes *remained at subnormal* values during the following month After about 40 50 days however a steady decrease was noted until the 100th day when no potentials at all could be recorded

The peak latency of the scotopic *b* wave first temporarily increased This increase corresponded to the initial decrease in amplitude After about 25 days a progressive reduction was recorded *After about* 60 days however the latency steadily increased to normal values

The latencies of the oscillatory potential increased slightly at first with a

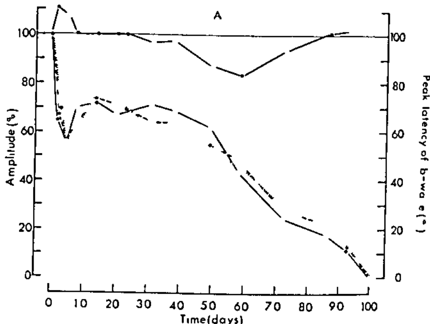


Fig 3A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 15 iron particles in the vitreous of a rabbit eye (implantation performed at zero on horizontal time axis)

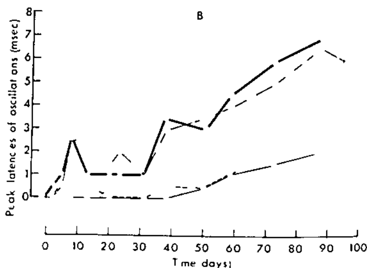


Fig 3B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o_2 broken line o_3 dotted line o_4 broken dotted line o_5 heavy solid line) of the oscillatory potential in the experiment described in Fig 3A When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

subsequent normalization after about 10 days Thirty days later a progressive increase of the latencies started This increase is illustrated in Fig 4 which shows the oscillatory potential at three stages of the developing retinal damage (A B and C in chronological order) The upper tracings were recorded from the test eye and the lower tracings from the intact eye *In Fig 4A the curves were recorded from an animal in which 8 particles were implanted in the right eye* Here a slight increase of the latencies can be seen and this increase is

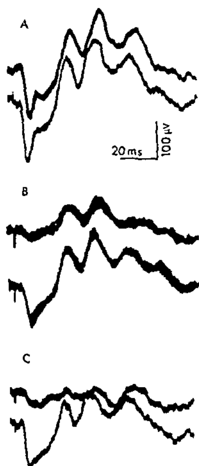


Fig 4
The oscillatory potential at three stages of developing retinal damage in *siderosis bulbi* (A B and C *in chronological order*) *Upper tracings* test eye *lower tracings* intact fellow eye

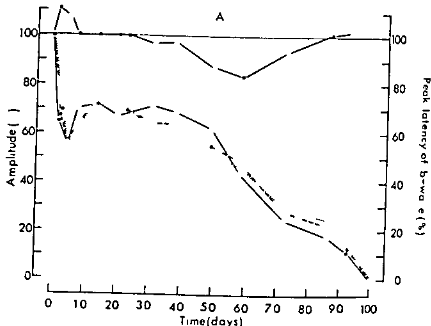


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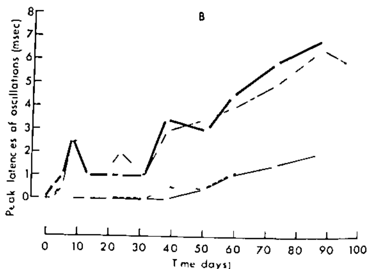


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weeks after the implantation and may represent an incipient atrophy of the retina

On ophthalmological examination special interest was paid to the vitreal reaction to the implanted particles This reaction is photographically illustrated in Fig 5 In all the photographs in this figure rounded intense white spots can be seen These represent photographic artefacts from reflexes in the lens system In Fig 5A the particles were photographed two hours after the implantation the particles are seen uncovered in the vitreous and one of the white broad of medullary fibers in the rabbit fundus is seen behind Two days after the implantation (Fig 5B) an incipient encapsulation of the particles was noted and after 10 days (Fig 5C) the encapsulation was maximal being formed by a white and diffusely delimited material From this moment on however the capsule slowly changed its appearance It became smaller more sharply delimited and changed its colour from white to yellowish white These capsule changes probably representing a resorption process continued until most of the particles were seen uncovered and glistening again (Figures 5D E and F are pictures taken 25 40 and 55 days after the implantation respectively) The development of the initial reversible decrease and the subsequent slow reduction of the ERG amplitudes might be due to changes in the concentration of toxic metal ions (or ion complexes) in the vitreous In fact this assumption is supported by the ophthalmoscopical findings Fig 6 shows that there is a temporal correlation between the electroretinographic changes and the capsule formation and resorption It is to be expected that the dissociation of the iron ions from the particles is maximal immediately after the implantation During this phase the amplitude of the ERG diminishes Then the ion dissociation steadily decreases partly because of the incipient encapsulation of the particles and partly because of the electrochemical equilibrium which is being established between metal area and the surrounding medium This decreased ion dissociation is the probable cause of the increase of the ERG recorded on the 10th day Electroretinographically the following period is characterized by a more or less constant amplitude at the end of this period the particles reappeared as a result of the capsule resorption (D F) From then on a progressive retinal deterioration occurred as judged by the reduction of the amplitude of the ERG The falling phase of the curve and the observed slow decapsulation of the particles indicate that the ion dissociation is slow during this phase

Injection of an iron salt solution into the vitreous As mentioned above the initial fast ERG changes can be referred to a sudden retinal exposure to a large number of iron ions or iron containing ion complexes originating from the metal after the implantation It is to be expected that a similar condition i e a sudden retinal exposure to a large number of ions should be obtained by the injection of a small quantity of an iron salt solution into the vitreous

In order to study the initial process more closely 0 1 cc of a 0 12 M solution

more pronounced in B and C which were recorded from the animal in which 15 particles were implanted (in B five curves are superimposed) In this connection mention should be made of the view that the oscillatory potential is generated by reverberating circuits in the outer plexiform and inner nuclear layers of the retina (see *e g Brown* 1968) The *b*-wave is also considered to originate in the inner nuclear layer although generated as a dipole extending through the layer *(Arden & Brown* 1965) For these reasons it is advisable to evaluate the oscillatory potential only in relation to the *b* wave and no attempts were made to measure *minor* quantitative differences in these oscillations In the experiment illustrated in Fig 3 for instance the oscillations diminished However there was also a concomitant reduction of the *b* wave In the final stage before the potentials disappeared the oscillations even dominated the ERG record (Fig 4C)

The electroretinographical findings illustrated in Fig 3 indicate that the development of retinal damage consists of two phases *viz* an initial temporary one followed by a slowly progressive one The initial changes comprise a reversible amplitude decrease a reversible increase of the *b*-wave peak latency and a moderate increase in the latencies of the oscillations The second phase which in this animal appeared after 40 50 days is characterized by a progressive decrease in the amplitudes and a progressive increase in the oscillatory potential latencies The *b*-wave peak latency first decreased but later reached normal values

On ophthalmological examination an aqueous flare was noted for the first five days after the implantation but not later One of the *clinical* siderotical manifestations in the anterior segment is a brownish pigmentation of the iris (see *Knave* 1969a) This was not found in the present rabbit experiment probably because of the intense brown colour of the rabbit iris which would render such an observation more difficult Nor were any clinical iris changes such as mydriasis or atrophy demonstrated Small pigment granules on the anterior surface of the lens were seen in the corneal microscope These granules appeared after a day or two and remained throughout the observation period Similar changes on the anterior surface of the lens were also observed for the rabbits in which 8 and 4 iron particles were implanted

The chinchilla rabbit normally exhibits a visible pigmentation of the retinal pigment epithelium The choroidal pattern for instance is obscured by pigment when viewing the rabbit fundus ophthalmoscopically Conspicious white broad bands of medullary fibers extending from a deeply cupped optic nerve head contribute to a variegated ophthalmoscopical picture This might be one of the reasons why no pigmentary retinal degeneration – easily seen in humans – were detected The only pathological finding the functional consequences of which are shown in Fig 3 was a peripherally more pronounced glistening reflex from the fundus at direct ophthalmoscopy This finding was first noted about 6

weeks after the implantation and may represent an incipient atrophy of the retina

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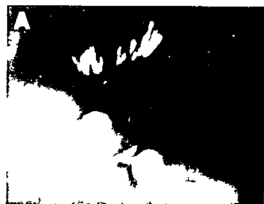












Fig 5

Photographs of iron particles in the vitreous two hours (A) two days (B) 10 days (C) 25 days (D) 40 days (E) and 55 days (F) after the implantation of 15 iron particles

of ferric chloride was injected intravitreally in a rabbit eye Fig 7 shows the electroretinographical results during the first hour after which time the eye was enucleated for histological examination As can be seen the *a* wave was

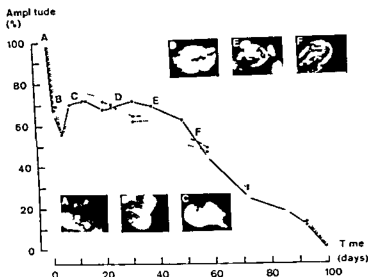


Fig 6

The ERG amplitudes following the implantation of 15 particles correlated to the appearance of the implanted particles The amplitude graph is taken from Fig 3A and the photographs (A F) from Fig 5

first unaffected but decreased slowly later on The *B* and *b* waves showed similar changes but the decrease appeared earlier and was more pronounced The peak latency of the scotopic *b* wave was first unaffected but later a minor increase was registered The latencies of the oscillatory potential did not change very much (see Fig 7B) the amplitudes however continuously dec reased and the oscillations were hardly discernible at the end of the experi ment. Fig 8 illustrates this amplitude reduction in the upper tracing which represents the test eye practically no oscillations are seen the lower tracing with normal oscillations represents the intact fellow eye

Implantation of 8 iron particles Eight iron particles were implanted in the right eye of two animals The results of these two experiments are shown in Fig 9 and 10

As can be seen in Fig 9 the results of which represent one animal an initial reversible amplitude reduction of the *a* and *b* waves was followed by a slower decrease (Fig 9A) After the 40 50th day however the amplitudes increased again and during the following 300 days remained stationary at the 60 70 per cent level After 500 days the amplitudes were found to be reduced to about 0 per cent During the first 60 days the *a* wave reduction was less than that of the *B* and *b* waves The *b* wave peak latency was slightly diminished up

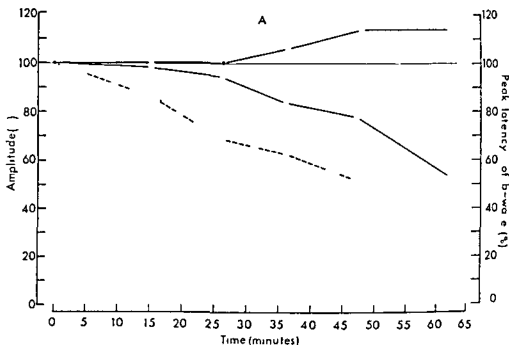


Fig 7A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the injection of 0 1 cc of a 0 12 M solution of ferric chloride in the vitreous (injection performed at zero on horizontal time axis)

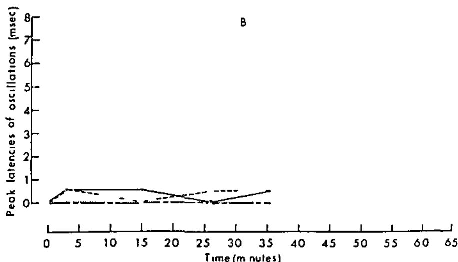


Fig /B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o broken line o_3 dotted line o_4 broken dotted line o_5 heavy solid line) of the oscillatory potential in the experiment described in Fig 7A When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye



Fig 8

The oscillatory potential recorded from an eye one hour after the intravitreal injection of 0 1 cc of a 0 1? M solution of ferric chloride *(upper tracing)* and at the same time recorded from the intact fellow eye (*lower tracing*) Time marking 10 msec Amplitude marking 50μV

to the 50th day when a relatively rapid decrease was obtained During the rest of the observation period a normalization and even an increase was noted

The latencies of the oscillatory potential increased moderately during the two first weeks reaching a maximum between the 30th and 60th day followed by a slight decrease (Fig 9B) The reduction of the *a* and *b* waves was also *maximal between the 30th and 60th day* Later *a progressive increase* in the latencies of the oscillations was noted

Ophthalmoscopically the changes in this eye were similar to those in the eye in which 15 particles had been implanted Thus the initial encapsulation was followed by a resorption of the capsule causing the particles to reappear The decapsulation occurred somewhat earlier and was more rapid than in the aforementioned experiment The glistening fundus reflex seen after 6 weeks in the 15 particle experiment and interpreted as a sign of incipient retinal atrophy was noted after 20 30 days in this experiment Thus in both experiments described the appearance of the glistening fundus reflex parallels the capsule resorption and is noted only after a prolonged ion exposure to the retina

When denuded some of the particles were seen to be fragmented The remains of the capsule were also fragmented into minute parts which were spread

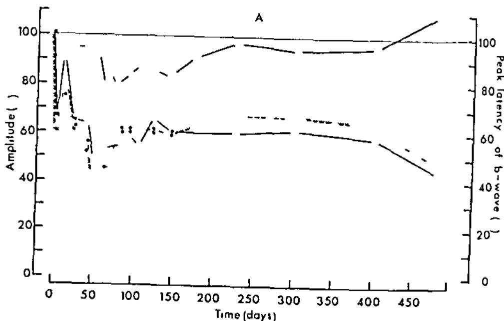


Fig 9A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 8 iron particles in the vitreous (implantation performed at zero on horizontal time axis)

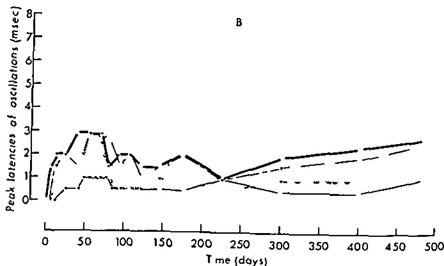


Fig 9B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o_2 broken line o_3 dotted line o_4 broken dotted line o_5 heavy solid line) of the oscillatory potential in the experiment described in Fig 9A When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

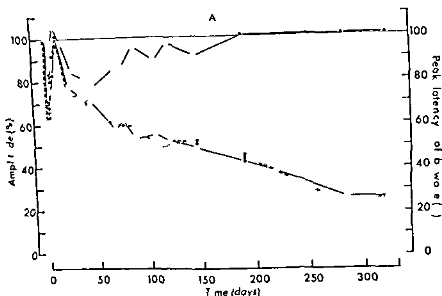


Fig 10A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation og 8 iron particles in the vitreous of *another* rabbit (implantation performed at zero on horizontal time axis)

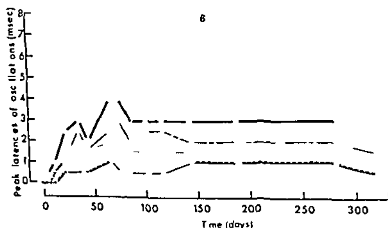


Fig 10B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o broken line o_3 dotted line o_4 broken dotted line o heavy solid line) of the oscilla ry potential in the experiment described in Fig 10A When affected these oscilla ons were always increased this increase is expressed in msec, the *reference being* the intact fellow eye.

in the vitreous together with small white wads many of which were lying pre retinally In this eye a retinal oedema also developed in a narrow sector peri pherally Therefore a rapid deterioration was expected to follow Instead an improvement occurred as judged by ophthalmoscopy The retinal oedema dis appeared as did some of the remains of the capsule It should be mentioned however that some of the preretinal wads persisted followed by local retinal atrophies The structural improvement which lasted for about a month was paralleled by an increase of the ERG amplitudes between the 60th and 90th day after the implantation (Fig 9A)

The appearance of the particles and their fragments slowly changed in the course of several months The smallest fragments disappeared entirely and the larger ones very slowly were *encapsulated again* Thus after about 200 days these particles were seen with a thin and gelatinous capsule The remains of the initial capsule also changed their appearance to sharply delimited yellow brown structures some of which formed the main parts of strands through the vitreous

Fig 10 shows the results following the implantation of 8 particles in the other rabbit The initial changes were similar to those described in Fig 9 but after about 40 days a slow progressive reduction of the *a*- and *b* wave oc curred The changes of the *b*-wave peak latency did not differ much from those illustrated in Fig 9A The latencies of the oscillatory potential (Fig 10B) showed a normalization trend after about 30 40 days At about 50 days *i e* concurrently with the reduction of the *a* and *b*-wave mentioned above these latencies increased again until about the 100th day whereupon the changes remained stationary for a long time In the final recording a slight decrease was noted

Ophthalmoscopically the essential difference between the experiments illu strated in Fig 9 and 10 was the appearance of a large retinal oedema in the latter case This oedema was visible in a narrow sector 50 days after the im plantation In the course of about a month the oedematous area grew larger to cover a broad sector between 2 and 8 o clock This oedema was more or less stationary throughout the rest of the observation period

Implantation of 4 iron particles Four iron particles were implanted in the right eye of two rabbits The results of these experiments are shown in Fig 11 No latency data are presented because they did not differ from those of the intact eye The upper curve (A) representing one of the experiments showed a slight decrease of the potentials the *b*- and *B*-waves being more reduced than the *a*-wave In the experiment illustrated by the upper curve an incipient encapsulation was noted two days after the implantation Four days later a de limited vitreal haemorrhage was also seen enclosing the encapsulated particles This haemorrhage was slowly resorbed and after about 100 days it could not be observed In its place about 15 small fragments of glistening metal appeared

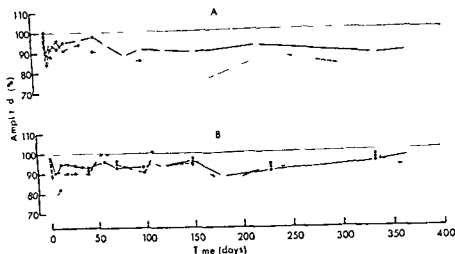


Fig 11

Amplitudes (*a* wave solid line *b* wave dotted line *B* wave broken line) expressed *in per cent of those of the intact fellow eye* following the implantation of 4 iron particles in the vitreous of the eyes of two rabbits (A and B) (implantation performed at zero on horizontal time axis)

The largest one of these fragments was slowly enclosed by a thin gelatinous capsule The others lost their glistening appearance and were reduced in number On the last examination only five very small fragments were seen A slight amplitude decrease appeared at about 60 days after implantation This decrease corresponded to the denudation of the metal fragments which probably resulted in an increased iron ion dissociation from the metal to the surrounding media (and thus to the retina) No further damage then occurred probably since the vitreal fluid turn over was now sufficient for the removal of dissociated iron ions from the particles the size of which had been reduced by corrosion

The lower record (B) of Fig 11 also shows slightly reduced amplitudes but in this respect no difference between the *a* and *b* waves was found No intravitreal haemorrhage was seen Encapsulation reactions similar to those described in the 8 particle experiments were observed

Discussion

The results of this study show that the encapsulation of the implanted particles plays an important role in the development of *siderosis bulbi* In the first days

in the vitreous together with small white wads many of which were lying preretinally In this eye a retinal oedema also developed in a narrow sector peripherally Therefore a rapid deterioration was expected to follow Instead an improvement occurred as judged by ophthalmoscopy The retinal oedema disappeared as did some of the remains of the capsule It should be mentioned however that some of the preretinal wads persisted followed by local retinal atrophies The structural improvement which lasted for about a month was paralleled by an increase of the ERG amplitudes between the 60th and 90th day after the implantation (Fig 9A)

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sent study might well correspond to some of the results presented by these authors Any comparison of the long term changes however cannot be done because their experiments were carried out during too short a time

From the results of many investigations (*Granit* 1933 1947 1955 *Noell* 1954 *Brown* & *Wiesel* 1961a b *Arden* & *Brown* 1965 *Brown* *Watanabe* & *Murakami* 1965) the *a* wave has been found to be generated in the photoreceptors and the *b* wave as a di pole extending through both the inner nuclear layer and inner plexiform layer hence the *b* wave probably is generated by the bipolar cells (*Arden* & *Brown* 1965) In the clinical studies the first pathological ERG change to appear was that of a type called *neg* + i e a pathologically increased *a* wave with a normal *b* wave (*Karpe* 1957 *Knave* 1969a) In the subsequent development the *a* wave persisted in most cases while the *b* wave decreased before the ERG became completely non recordable Thus the clinical investigations indicate that the receptor cells retain function longer than the bipolar cells This is in agreement with the histological picture of early ganglion cell changes and late receptor cell changes (see *e g* *Duke Elder* 1954)

That the ganglion cells are destroyed earlier than the receptor cells can be explained by the fact that the metal ions reach the retina from the vitreous and that the parts lying more vitreally are then attacked first. In the present rabbit study no consistent difference between the *a* and *b* wave was found in the eyes in which iron particles were implanted This might be due to the fact that the rodent retina is thinner than that of man (*Detwiler* 1943) so that the toxic iron ions reach the ganglion cells and the receptor cells at about the same time This theory might be supported by the ERG findings immediately after the intravitreal injection of the iron chloride salt solution the *b* wave was found markedly reduced and the *a* wave more or less intact The histopathological changes of that eye were mainly found in the neuronal part of the retina with no changes found in the receptor cells (*Knave* & *Kock* 1969)

In this connection it should be pointed out that in some of the siderotical eyes of the clinical study (*Knave* 1969a) both the *a* and *b* wave were found reduced i e the ERG was *subnormal* On the other hand a slowly developing purely negative ERG was also obtained in a rabbit after the implantation of aluminium particles in the vitreous (*Knave* 1969d) Thus it is very probable that local conditions in the retina and the amount and rate of toxic ions reaching the retina are mainly responsible for the development of the different types of ERG in *siderosis bulbi* The reaction of different cell types to the metal ions may also be a contributory factor

It seems reasonable to suggest that the initial changes may be due to a retinal oedema caused by the heavy dose of toxic iron ions reaching the retina. The second slow phase probably is due to a slowly developing retinal atrophy without the involvement of any oedema Some results of other authors support this suggestion Thus an amplitude reduction of the oscillatory potential in connec

after the implantation a white and diffuse capsule is produced This capsule then slowly diminishes and turns yellow At the same time the particles re appear First they can be seen as dark spots in the capsule and later the glisten ing metal is seen A second thinner capsule appears much later after several months

To the author s knowledge this double encapsulation process has not been described before *Leber* (1891) on the basis of experiments on rabbits described the initial encapsulation On the basis of experiments with rust particles he also described the disappearance of the initial white capsule It is also known that encapsulated particles after a long time may change their location and then cause inflammation *(Duke-Elder* 1954) It has been claimed that the capsule material is derived from organized hemorrhage and that this material tends to undergo atrophy and dissolution because of the heavy dose of toxic metal ions (Atlas and Textbook of Ophthalmic Pathology 1957) This theory is not sup lorted by the results of the present investigation The present results indicate that the encapsulation process is mainly due to the reaction of the vitreous sub stance to the particles and is not related to any haemorrhage

As pointed out the present results indicate two phases in the development of siderotical changes in the retina The initial phase is probably related to the sudden exposure to the retina of a heavy dose of metal ions immediately after the implantation of the particles and is characterized by the following ERG findings (1) a partly reversible reduction of the *a*- and *b*-wave amplitudes (2) a normal or even a slightly increased *b* wave peak latency and (3) a slight or *moderate increase of the latencies of the oscillations of the oscillatory* potential In the second phase (1) a slowly progressive *a*- and *b* wave amplitude reduc tion was recorded together with (2) a progressive increase of the latencies of the oscillations The *b* wave peak latency (3) in this phase first decreased but later was normalized and sometimes even increased a little These slow changes probably are due to the prolonged slow dissociation of iron ions in connection with the capsule resorption

The initial phase was studied more closely by injecting an iron salt solution into the vitreous The resulting ERG findings were similar to those recorded in the initial phase and in addition an amplitude reduction of the oscillatory po tential was found after an hour the oscillations were hardly discernible

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As mentioned in the introduction the ERG following the intraocular implantation of iron pieces has been studied in the rabbit *Sugita et al* (1960) inserted iron pins (8 × 1 mm) and *Seto* (1960) iron particles 3 × 0 75 mm) into the vitreous The resulting ERG changes were followed for a short time only one and two months respectively Sugita et al reported that the *b* wave of the ERG either increased was normal or decreased Seto on the other hand found that the *b*- and *c*-waves decreased day by day In both works a trend of the *b*-wave latency to increase was reported The initial changes found in the pre

upon the size of the metal area, the particles reappeared About half a year of a year later however a new thinner capsule slowly developed

A temporal correlation between the ERG changes and the capsule formation and resorption was demonstrated During the first days after the implantation the following changes were recorded (1) a reversible *a* and *b* wave amplitude reduction (2) a normal or a slightly increased peak latency of the scotopic *b* wave and (3) a moderate increase of the peak latencies of the oscillations of the oscillatory potential These changes probably are to be ascribed to a retinal oedema as a result of the sudden exposure of a heavy dose of iron ions dis sociated from the metal just after the implantation By injecting an iron chlo ride solution into the vitreous a similar condition i e a retinal oedema was obtained In addition to the changes accounted for above an obvious amplitude reduction of the oscillatory potential was recorded

In connection with the reappearance of the iron particles slow progressive ERG changes were recorded (1) an *a* and *b* wave amplitude reduction and (2) a marked increase of the peak latencies of the oscillations The *b* wave peak latency (3) first decreased but later was normalized and sometimes even in creased a little. A reduction of the amplitude of the oscillatory potential was found to occur This reduction however was not more pronounced than that of the *b* wave In the final recordings before the potentials disappeared these oscillations even dominated the records

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tion with a retinal oedema and/or a posterior uveitis has been reported in man (*Yonemura et al* 1962) and in pigeon (*Algvere et al* 1968) Although not directly supporting the abovementioned theory a similar increase of the *b* wave peak latency in connection with a corresponding amplitude reduction has been reported after thrombosis of the central retinal vein in man (*Muller & Haase* 1968) and after raising the intraocular pressure in the rabbit eye (*Bornschein & Zwiauer* 1952)

In intraretinal microelectrode experiments (see *e g Brown* 1968) the maximal amplitudes of the oscillatory potential were found in the inner nuclear and outer plexiform layers and the oscillations were considered to be generated from reverberating circuits in the feed back mechanisms of the retinal neuronal network This concept on the origin of the oscillatory potential might well agree with the findings of the present work *viz* reduced oscillations in eyes with a retinal oedema and preserved oscillations in eyes with a slowly progressive retinal atrophy due to siderosis In retinal oedema the intercellular space will expand and the cells will be pushed away from each other causing a deterioration of the intercellular connections Thus the basic mechanisms of the oscillatory potential are damaged and the oscillations will be less pronounced The atrophy in retinal siderosis mainly involves the peripheral parts of the retina (see *Duke-Elder* 1954) the central parts being left preserved The ERG potentials generated from this preserved central field probably are shunted by the degenerated tissue of the peripheral retina and will thus be diminished at the active electrode on the cornea (*Karpe* 1948) It is to be expected that the oscillatory potential will be reduced in the same way and by the same order of magnitude as the *B* or *b* wave This is what was found in the present study

However *Yonemura et al* (1962) reported that the oscillatory potential usually "disappeared" in *siderosis retinae* and *Algvere* (1968) found extinguished" oscillations in one case of siderosis In two additional cases modified" oscillations were reported (*Perdriel et al* 1964) Many factors may be responsible for the differences between these results and those of the present study *e g* extent and type of siderotic damage difference in recording techniques etc

Summary

The ERG and ophthalmological changes following the implantation of pure iron particles in the vitreous were studied in long term experiments in the rabbit

The particles were encapsulated soon after the implantation After about a week the capsule began to resorb and after a varying period of time depending

upon the size of the metal area the particles reappeared About half a year or a year later however a new thinner capsule slowly developed

A temporal correlation between the ERG changes and the capsule formation and resorption was demonstrated During the first days after the implantation the following changes were recorded (1) a reversible *a* and *b* wave amplitude reduction (2) a normal or a slightly increased peak latency of the scotopic *b*-wave and (3) a moderate increase of the peak latencies of the oscillations of the oscillatory potential These changes probably are to be ascribed to a retinal oedema as a result of the sudden exposure of a heavy dose of iron ions dissociated from the metal just after the implantation By injecting an iron chloride solution into the vitreous a similar condition i e a retinal oedema was obtained In addition to the changes accounted for above an obvious amplitude reduction of the oscillatory potential was recorded

In connection with the reappearance of the iron particles slow progressive ERG changes were recorded (1) an *a* and *b* wave amplitude reduction and (2) a marked increase of the peak latencies of the oscillations The *b* wave peak latency (3) first decreased but later was normalized and sometimes even increased a little A reduction of the amplitude of the oscillatory potential was found to occur This reduction however was not more pronounced than that of the *b* wave In the final recordings before the potentials disappeared these oscillations even dominated the records

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THE ERG AND OPHTHALMOLOGICAL CHANGES IN EXPERIMENTAL METALLOSIS IN THE RABBIT

II Effects of steel copper and aluminium particles

BY

BENGT KNAVE

Introduction

Retained intraocular metal particles can give rise to tissue damage in the different parts of the eye called *metallosis bulbi* Retinal damage occurs at an early stage and is the most detrimental results of metallosis This damage has been studied by means of ERC in clinical works (*Karpe* 1948 1957 *Schmoger* 1956 *Straub* 1961 *Ko ousek* 1965 *Knave* 1969a)

In the clinical investigation by *Knave* (1969a) the results indicated that *minor* differences in the alloy content of steel particles might be important for the occurrence of siderosis bulbi This has been studied more closely in the rabbit in the present work which also can be regarded as a complement to a recent investigation on the long term effects following the implantation of pure iron particles into the rabbit vitreous (*Knave* 1969b) Moreover the ERG following the intravitreal implantation of copper and aluminium particles has also been studied in the present work since this has not been done before and since particles of copper and aluminium next to those of iron and steel are the most commonly occurring intraocular metal foreign bodies in the human eye

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The ERG method as well as the ophthalmological examination and implantation techniques have been described elsewhere (*Knave* 1969b, c)

The composition of the implanted steel particles (Sandvik) is presented in Table I

The different alloys were chosen for various reasons In the clinical study by the author (*Knave* 1969a) the particle size and location were almost identical in two cases In one of these cases there were no signs of siderosis 10 months after the accident when the particles entered the eye in the other case advanced siderotical changes appeared after only 5 months The main difference between these cases was the alloy content of the particles in the first mentioned case the particle contained 5 % nickel in the second mentioned only 1 % Because of this difference 2XN5 steel particles were implanted in order to be able to compare the resulting changes with those reported in another study where pure iron particles were implanted (*Knave* 1969b) The 6R60 6C27 and HT2 steels are stainless with a varying degree of corrosion resistance the 6R60 steel is highly corrosion resistant All the steels presented in Table I as well as the corrosive carbon steels *i e* iron alloyed with minor quantities of carbon are used in different tools depending upon their specific properties.

The implanted copper particles (Mallinckrodt) had a copper content of 99 8 per cent and the aluminium particles (KEBO) an aluminium content of 96 97 per cent

All the implanted particles were cubes with a side of 0 4 0 5 mm This was also the case with the pure iron particles the implantation of which was described in another work (*Knave* 1969b)

The present study reports the results of long term experiments in which steel copper and aluminium particles were implanted in the vitreous of the right eyes of seven rabbits Four rabbits received 15 steel particles each one received 15 aluminium particles The number of 15 was chosen in order to be

Table I
The composition (in per cent) of the implanted steel particles

Steel	Cr	Ni	Mo	Si	Mn	C	Fe
2XN5		5 2		0 1	0 4	0 1	94 [illegible]
HT2	5 0			1 9	0 2	0 1	92 8
6C27	14 0			0 2	0 3	0 3	85 2
6R60	17 8	12 3	2 8	0 6	1 5		64 [illegible]

able to compare the present results with those reported in another study where 15 particles of pure iron were implanted (*Knave* 1969b) When implanting copper particles however the vitreous reaction was found to be intense enough following the implantation of 8 particles and in the seventh animal therefore only 4 copper particles were implanted In all experimental series the left eye served as normal reference (see *Knave* 1969b)

Results

Implantation of differently alloyed steel particles

a) *5% Ni steel* In one of the experiments 15 steel particles (2NX5) containing 5% nickel were implanted The ERG results of this experiment are presented in Fig 1 Fig 1A shows the resulting changes in amplitudes (filled circles) and the scotopic *b* wave peak latency (squares) expressed in per cent of the values for the intact fellow eye The *a* wave amplitude is represented by a solid line the *b* wave by a dotted line and the *B* wave (measured from the peak of the *a* wave to the peak of the *b* wave) by a broken line Fig 1B shows the peak latencies of the first five positive oscillations of the oscillatory potential (triangles O_1 O_2 O_3 O_4 and O_5) When affected these latencies always were found to increase This increase is expressed in msec compared to the latencies of the intact fellow eye

As can be seen in Fig 1A the amplitudes of the potentials rapidly decreased after the implantation After a couple of days however they increased to a subnormal level of about 50 60 per cent between the 25th and 65th day During the following 4 months a slow reduction occurred From about the 190th day the amplitudes were found to be subnormal at the 20 per cent level

The scotopic *b* wave peak latency did not change until 18 days after the implantation when subnormal values were recorded *After 25 days the latency* was found to be 70 per cent of that of the intact fellow eye From then on however the latency started to increase and reached normal values after 150 days

The latencies of the oscillatory potential were moderately increased during the first 20 30 days During the following month a slight trend towards normal values was noted but this trend was interrupted by a new very slow increase from the 60th day The amplitude of the oscillations diminished concurrently with the *b* wave amplitude and by the same order of magnitude

Ophthalmological examination showed that there were insignificant changes in the anterior segment An aqueous flare was noted during the first week after implantation A slight pigment granulation on the anterior lens capsule was

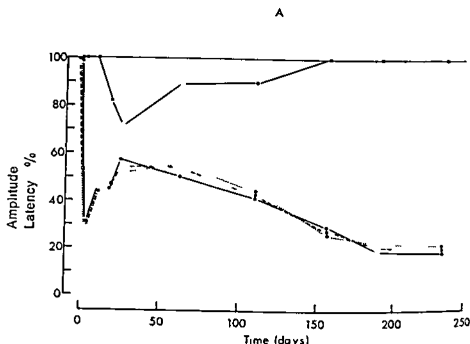


Fig 1 A

Amplitudes (filled circles) af *a* wave (solid line *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 15 steel particles alloyed with 5 % Ni Implantation performed at zero on horizontal time axis

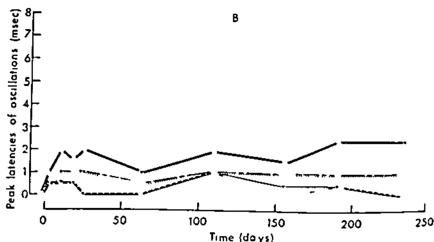


Fig 1B

Peak latencies of the five first positive oscillations of the oscillatory potential (o_1 thin solid line *o* broken line o_3 dotted line o_4 dotted broken line *o* heavy solid line) of the ERG in the experiment described in Fig 1A

seen in the corneal microscope as the only pathological finding of the anterior segment throughout the rest of the observation period

Special interest was paid to the reaction of the vitreous substance to the im planted particles A *day or two after the implantation* a capsule was formed around the particles This capsule was white and diffusely delimited and was maximal at about the 10th day From then on a slow progressive resorption of the capsule occurred About 60 days after the implantation most of the particles were seen as glistening metal After about 160 days a new encapsulation pro *cess was detected this second capsule being much thinner than the first* one persisted throughout the rest of the observation period

At the same time as the initial capsule was formed small white wads were seen in the vitreous Most of these wads were later resorbed Some of them though persisted and were located preretinally which gave rise to local retinal atrophies seen toward the end of the experiment It should also be mentioned that remains of the initial capsule persisted forming the main parts of strands extending through the vitreous Moreover at direct ophthalmoscopy a *glisten ing* reflex from the peripheral parts of the fundus could be seen from about the 30th day This glistening reflex persisted until the end of the experiment

In this experiment there was a temporal correlation between the ERG chan ges and the capsule formation and resorption in the same way as was shown *photographically in experiments in which pure iron particles were implanted* (*Knave* 1969b) Thus for the 5 % Ni steel one may conclude that just after the implantation the retina is exposed to a sudden and heavy dose of toxic iron ions which results in a decrease of the ERG This decrease is reversible and is assumed to be due to a diminishing ion dissociation following the encapsula tion of the particles When the particles are slowly decapsulated the ERG again decreases At the end of the experiment a new capsule develops which *probably accounts for the* constant amplitudes recorded during the last 45 days In the above mentioned study (*Knave* 1969b) the *initial reversible* ERG *chan* ges were suggested to represent a retinal oedema while the later progressive ERG changes were assumed to be due to a retinal atrophy

b) 5 % Cr steel *In this experiment* 15 steel particles (HT2) containing 5 % chromium were implanted The resulting ERG changes are shown in Fig 2A No latency data are presented because they did not differ from those recorded in the intact fellow eye As can be seen in the diagram an initial reversible re duction was recorded during the first 10 days the *b* wave being more reduced than the *a* wave From then on during the rest of the experimental period the *a* wave was found normal The *b* and *B* waves were found slightly increased between the 1[illegible]0th and 180th day *From* then on they decreased and reached subnormal values after 300 days This decrease was slightly more pronounced 400 days after the *implantation*

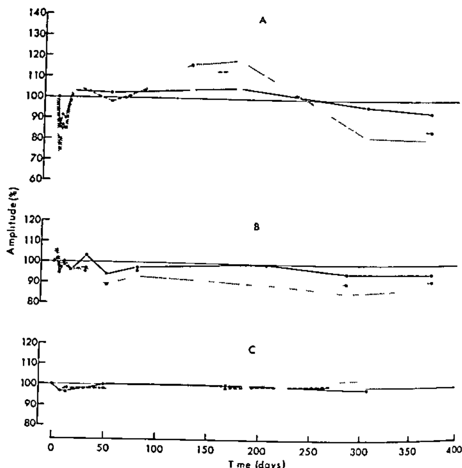


Fig 2

Amplitudes of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) of the ERG following the intravitreal implantation of 15 steel particles alloyed with 5 % Cr (A) 14 % Cr (B) and 18 % Cr 12 % Ni 3 % Mo (C) Implantation performed at zero on horizontal time axis

The reaction of the vitreous substance to the implanted particles in this experiment differed from that of the preceding one After about 10 days a thin white yellow coating was seen to cover parts of the particles This coating very slowly diminished and after about 130 days most of the particles were seen uncovered a condition that remained constant during the remaining observation period It should be mentioned that a few preretinal wads were noted between the 100th and 200th day after which time they could not be detected Moreover in contrast to the experiments where iron or 5 % Ni steel particles were implanted no glistening reflex was seen

c) 14 % Cr steel In this experiment 15 steel particles (6C27) containing 14 % chromium were implanted The resulting FRG changes are shown in Fig 2B Like the experiment where 5 % Cr steel particles were implanted no latency data are presented because they did not differ from those of the intact fellow eye As can be seen in the diagram the resulting changes of the amplitudes are within normal limits (see *Knave* 1969b) although the *b* wave constantly was recorded somewhat more reduced than the *a* wave

Ophthalmoscopically the particles were seen glistening and quite uncovered up to the last observation when a very thin white coating partly covered some of the particles A couple of very small wads were seen in the vitreous between the 100th and 200th day but not later After the 200th day a very slight glistening fundus reflex was seen in the lower parts of the fundus

d) 18 % Cr 12 % Ni 3 % Mo steel In one eye 15 particles of this highly corrosion resistant steel (6R60) were implanted Fig 2C shows that the ERG potentials of this eye did not differ from those of the intact fellow eye. Ophthalmoscopically a thin coating partly covering some of the particles was detected at about the 1/0th day This coating was found to be increased after 300 days No glistening fundus reflex or vitreal wads were noted in this experiment.

Implantation of aluminium particles

In one experiment 15 aluminium particles were implanted The resulting ERG changes are shown in Fig 3 As can be seen in Fig 3A the amplitudes first decreased temporarily The *a* wave was then found to increase between the 10th and 20th day normal values being reached 40 days after the implantation The *b* and *B* waves were subnormal the first 20 days and on the 40th day normal values were again recorded From the 40th day on the amplitudes diminished slowly There was a conspicious difference between the reduction of the *a* wave and that of the *b* and *B* waves the latter ones being considerably more reduced At the end of the experiment the *b* wave approached zero while the amplitude of the *a* wave still remained at about 90 per cent of the amplitude of the intact fellow eye

Following an initial reversible increase the peak latency of the *b* wave was found to increase slowly after the 140th day As seen in Fig 3B the latencies of the oscillatory potential were also found to increase slowly after the 140th day The amplitude of the oscillatory potential was found to be reduced to the same extent as the reduction of the *B* wave.

Ophthalmologically only insignificant changes occurred The particles were seen uncovered except during the last months of the experiment when a thin white coating developed covering parts of some of the particles

A

Amplitude Latency %

120, 100, 80, 60, 40, 20, 0

0, 50, 100, 150, 200, 250, 300, 350, 400

Time (days)

Fig 3A

Amplitudes (filled circles) of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 15 aluminium particles Implantation performed at zero on horizontal time axis

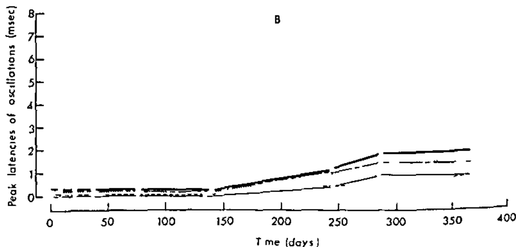


Fig 3B

Peak latencies of the five first positive oscillations of the oscillatory potential (o_1 thin solid line o broken line o_3 dotted line o_4 dotted broken line o_5 heavy solid line) of the ERG in the experiment described in Fig 3A

Implantation of copper particles

a) Implantation of 8 copper particles In this experiment only 8 particles were implanted since copper is known to be very toxic to the tissues of the eye (see Knave 1969a) The resulting ERG changes are presented in Fig 4 The *a*- and *b* wave amplitudes (Fig 4A) rapidly decreased during the first three days after implantation During the following two weeks the decrease continued but at a considerably slower rate Between the 15th and 35th day more or less constant subnormal amplitudes were recorded at a level between 25 and 40 per cent It should also be mentioned that throughout this experiment the *a* wave was found to be less reduced than the *B* and *b* waves From the 35th day a new reduction occurred until the 57th day when no potentials could be recorded

The *b* wave peak latency first increased slightly After a couple of days a decrease to subnormal values occurred This decrease was slowly reversible normal values were reached at the end of the experiment

The latencies of the oscillations of the oscillatory potential (Fig 4B) did not change during the first five days but during the following ten days an increase was noted During the remaining experimental period there was again a low increase The amplitudes of the oscillations were reduced by the same order of magnitude as the *B* and *b* waves

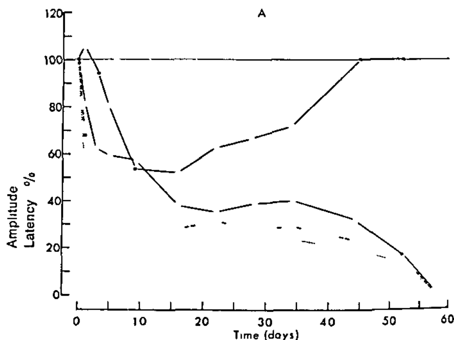
An aqueous flare was visible during the first two weeks Pigmented granules on the anterior lens capsule however could be seen from the first day after the implantation to the last day of observation

A dense thick yellowish white capsule was formed around each particle Some of the particles located peripherally were fully encapsulated after a few days The encapsulation of particles located centrally in the vitreous was slower and was not completed until two weeks after the implantation

One day after the implantation a diffuse white blue opacity was discernible as a thin veil in large parts of the vitreous This diffuse opacity changed after some days it became more white and delimited and after about two weeks it was divided into parts some of which formed strands extending through the vitreous After the same time i e after about two weeks a glistening reflex from the fundus could be seen at direct ophthalmoscopy This pathological reflex persisted to the end of the experiment

The capsules around each copper particle appeared as yellowish white balls in the vitreous After a month some of these capsules were seen ruptured with capsule material spread in the vitreous At least one copper particle was seen partly decapsulated with the metal glistening During the last weeks the vitreal opacities successively increased and a posterior cortical cataract was also seen at the end of the experiment.

There is a temporal correlation between the electroretinographical and ophthalmological changes The initial capsule formation may thus account for the



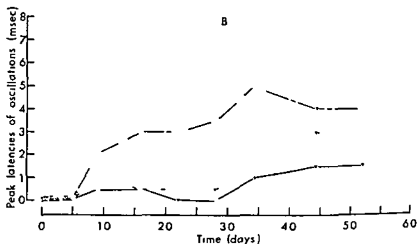


Fig 4A

Amplitudes (filled circles) of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 8 copper particles Implantation performed at zero on horizontal time axis

Fig 4B

Peak latencies of the five first positive oscillations of the oscillatory potential (o_1 thin solid line o broken line o_3 dotted line o_4 dotted broken line o_5 heavy solid line) of the ERG in the experiment described in Fig 4A

interruption at the 10th day of the initial ERG decrease The rupture of the capsules seen at the 30th day with the subsequent deterioration of vitreal structure probably accounts for the final ERG reduction

b) Implantation of 4 copper particles Because of the intense reaction in the eye after the implantation of 8 copper particles only 4 particles were implanted in this experiment Fig 5 shows the resulting ERG changes No latency data are presented because they did not differ from those of the intact fellow eye As can be seen in the diagram a sudden increase was recorded after about 10 days This increase was reversible normal values being reached after about 100 days From then on however a new reversible increase was recorded This time the normal values were not reached until 200 days later i e 300 days after the implantation During the remaining experiment period normal values were obtained When the ERG was found increased the *b* and *B* waves always were more increased than the *a* wave

On ophthalmological examination the particles were found encapsulated a few days after the implantation The diffuse white blue opacity seen as a thin veil in the vitreous in the preceding experiment was also seen in this experiment However it was only seen in a narrow sector surrounding all the particles and it disappeared after three weeks

Very small and highly glistening particles were seen in the vitreous 300 days

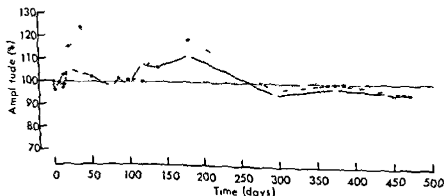


Fig 5
Amplitudes of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) of the ERG following the intravitreal implantation of 4 copper particles Implantation performed at zero on horizontal time axis

after the implantation The glistening particles increased in number during th
remaining experiment period

The capsules seen as yellowish white balls in the vitreous changed the colour toward yellow after 300 days Moreover after 400 days one of the capsules was seen clearly diminished so that the contours of the particle wer visible

Discussion

The general course of ERG changes as well as the ophthalmological changes following the implantation of steel particles alloyed with 5 % Ni were similar to the changes after the implantation of pure iron particles (*Knave* 1969b) i e the results indicate an initial reversible oedema followed by a progressive atrophy of the retina After the implantation of pure iron particles the ERG was non recordable after 100 days This detrimental course however did not occur in the 5 % Ni experiment After 100 days the ERG amplitudes were still 45 % of those obtained in the intact fellow eye and after 230 days a 20 % response remained These results thus confirm the clinical study (*Knave* 1969a) *viz* that even minor differences in the alloy content of the steel particles may influence the development of *siderosis bulbi*

The implantation of steel particles alloyed with 5 % Cr resulted in electroretinographical and ophthalmological changes entirely different from those recorded after the implantation of pure iron particles and particles alloyed with 5 % Ni Initially a thin coating covered the particles This coating diminished and after about 130 days most of the particles were seen uncovered At this time and some months later a slight *increase* of the *b* wave was recorded An increased ERG response was also recorded after the implantation of 4 copper particles In that experiment all the potentials were increased the *b* wave however more than the *a*-wave

It should be mentioned that in some of the clinical studies an increase of the ERG response has been described (see *e g* *Karpe* 1957 and *Knave* 1969a) as an early manifestation of *metallosis bulbi* The increased ERG potentials recorded in the present work (Fig 2A and Fig 5) probably represent an early manifestation of retinal metallosis too

The implantation of corrosion resistant steel particles (14 % Cr and 18 % Cr 12 % Ni 3 % Mo) did not induce any significant changes There was only a very slight reduction of the ERC in the 14 % Cr experiment and no changes in the ERG were noted in the other experiment The conclusion is that the dif

ference following the implantation of iron and steel particles depends on a lower iron ion dissociation rate of the steel particles The development of a slight coating on some of these particles and the appearance of a pathological glistening reflex from the fundus at ophthalmoscopy are in agreement with the view stated by *Duke Elder* (1954) that inert foreign bodies cannot be regarded as harmless to the eye

In the clinical study by the author (*Knave* 1969a) most of the eyes with retinal metallosis showed a *b* wave reduction that was more pronounced than that of the *a* wave In some eyes however the *a* and *b* waves were equally reduced. Therefore the experiment in which 15 aluminium particles were implanted is of special interest since in this experiment the *b* wave was considerably more reduced than the *a* wave A similar tendency was also noted in the above mentioned steel experiments where particles alloyed with 5 and 14 % Cr were implanted In the experiments where particles of pure iron and particles alloyed with 5 % Ni were implanted this difference did not exist These findings indicate that the retinal exposure to a heavy dose of toxic metal ions results in an ERG where the *a* and *b* wave are equally reduced A probable explanation is that the *a* and *b* wave generating structures are reached at about the same time by the toxic metal ions The finding that a prolonged exposure to a moderate dose of ions results in ERGs in which the *b* wave is more reduced may depend on the fact that the ions reach the structures that generate the *b* wave before they reach those generating the *a* wave (see *Knave* 1969b) This may also explain why the *b* wave was found more reduced than the *a* wave in the 8 copper particle experiment

Intravitreal copper particles are known to give rise to a rapidly developing detrimental eye damage (see *e g Duke Elder* 1954) This also occurred in the present study after implanting 8 copper particles in the vitreous of a rabbit eye The resulting ERG and ophthalmological changes indicated the existence of two phases in the development of the retinal damage (1) an initial phase which may be due to an oedema and (2) a later one which is assumed to be due to a slowly developing retinal atrophy

As mentioned above the implantation of 4 copper particles was followed by a long lasting increase of the ERG (especially of the *b* wave) This supernormal ERG may be the first and only sign of retinal metallosis in this case *Straub* (1961) after implanting a brass particle in the anterior chamber in two rabbit eyes also found the *b* wave to be reversibly increased

According to *Duke Elder* (1954) highly brilliant deposits in the fundus represent one of the characteristic reactions to retained intraocular copper particles In the 4 copper particle experiment a similar finding was noted very small highly glistening particles were seen in the vitreous 300 days after the implantation Because of their small size it was not possible to estimate their nature

Summary

In the present work the ERG and ophthalmological changes were studied following the implantation of steel, aluminium and copper particles in the vitreous of the rabbit eye.

Minor differences in the alloy content of the implanted steel particles were shown to play an important role in the development of *siderosis bulbi*. The results after implantation of steel particles alloyed with 5 per cent nickel resembled those obtained in another study where pure iron particles were implanted (*Knave* 1969b).

In three rabbits steel particles alloyed with (1) 5 % Cr, (2) 14 % Cr and (3) 18 % Cr-12 % Ni 3 % Mo were implanted. In the first mentioned of these experiments a long lasting reversible increase of the ERG was recorded, the *b*-wave being more increased than the *a*-wave. This increase was followed by a slight decrease, the *b*-wave being more reduced than the *a*-wave. In the second mentioned experiment a slowly developing small reduction of the ERG was observed; also here the *b*-wave was more reduced than the *a*-wave. In the third-mentioned experiment normal ERGs were recorded.

The encapsulation reactions to these three alloys also differed from those observed after implantation of pure iron particles. Only a thin coating developed covering parts of the particles. In the second- and third-mentioned experiments this coating was noted as late as 10–14 months after the implantation.

The implantation of aluminium particles resulted in a slow reduction of the *b*-wave so that after about 300 days practically no *b*-wave was obtained. The *a*-wave on the other hand was only reduced to 90 per cent. Only slight ophthalmological changes were noted, *e.g.* a partial thin coating of some of the particles at the end of the experiment.

In two eyes copper particles were implanted. The toxicity of copper ions resulted in a rapidly developing vitreal damage and deterioration of the ERG. The implantation of a reduced number of particles resulted in an increased ERG response recorded for long periods and interpreted as an early manifestation of retinal metallosis.

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Report of the Norwegian Ophthalmological Society s Annual Meeting November 1968

Weidemann J *Lowes Occulocerebral syndrome*

One year ago the author reported a similar case a boy who later died The mother remarried and now has a girl with the same disease There was microphthalmus on the left side and cataract on both sides There were also signs of kidney and brain damage Chromosomal testing showed female It is usually always boys who are affected by this disease

Hvidsten Hanne *Cortisone treatment of malignant exophthalmos – a case report*

Eleven patients were reported with exophthalmos treated with large doses of steroids Seven patients showed considerable improvement during the first weeks The subjective complaints particularly were reduced However recession measured with the exophthalmometer was more uncertain

Discussion *Waalen* asked whether anyone had experience with ismelin *Ytterbor* replied that ismelin might be of some help on the retraction of the eyelids but scarcely on the exophthalmos itself Many patients felt that the drops burned unpleasantly *Roe and Maartmann Moe* mentioned the strongly swinging tension values frequently found in exophthalmic eyes that were almost certainely due to technical difficulties with the tonometry *Thomassen* mentioned the difficulties of judging the results of the treatment of malignant exophthalmos since the degree of exophthalmos follows a rising curve spontaneously sinking He said that by the use of large doses of corticosteroids he really had the feeling for the first time that the treatment was effective *Horn* Some patients with malignant exophthalmos first come for treatment when they have large corneal ulcers and cortisone treatment is then questionable The question is then whether pressure relieving operation like the Kronlein s operation is indicated *Bertelsen* had never seen such a serious case that had really indicated such a drastic operation

Haugen H N *Cortisone treatment of exophthalmos*

First the two types of exophthalmos were mentioned i e the non infiltrative benign and the infiltrative malignant In the latter case it is not an excess of thyroid stimulat

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ng hormone but pathological amounts of long acting thyroid stimulator (LATS) and exophthalmos producing substance The treatment of this latter group of patients has so far been very unsatisfactory However large doses of corticosteroids seem to be effective Initial doses of 100 120 mg Prednisolon are recommended

The doses are reduced as quickly as possible The treatment gives not only a subjective effect because the concentration of LATS is considerably reduced Some cases need a continuing dose of 10 12 5 mg Prednisolon over a long period A discussion followed on the indications for operative treatment by the method of Kronlein or Naffziger

The diagnosis endogenous exophthalmos is difficult in one sided cases On a question from Ytteborg the speaker replied that one would probably always find pathological uptake values with a suppression or stimulation test if an endogenous exophthalmos was present

G j o n e E *Familial plasma cholesterol ester deficiency*

60% of cholesterol is found as ester Cholesterol reacts with a fatty acid lecithin Free cholesterol is found in all the cells of the body however it is deposited in the vessel wall as ester Three sisters were reported lacking the enzyme LCAT (Lecithin cholesterolacyltransferase) They had low concentrations of lysolcitin and cholesterol ester and practically all cholesterol was unbound

The disease was manifested by slight proteinuria normochromous anemia milk like plasma and low concentration of alpha pre beta lipoprotein The erythrocytes had a peculiar look because of the high cholesterol content and foam cells were found in the bone marrow and by kidney biopsy The most striking clinical sign however was corneal changes to be described by the next speaker

B e r g a u s t, B *Corneal changes with familial plasma cholesterol ester deficiency*

The three above mentioned sisters were examined ophthalmologically Their ages were 1 3? and 34 years They had no history of eye troubles and their vision was n rmal The same corneal changes were found in all three by slit lamp examination There was tiny gray dotted opacities centrally in the cornea then a clear intermediate zone and peripherally denser opacities almost resembling an arcus senilis Cholesterol was prol ably deposited in the cornea

V a l e b j o r g H *O intra cular feedback mechanisms by intraocular pressure and n the phys logical basis for the method of tonography*

Rabb t experiments were reported in which the blood vessels in the ciliary processes were inspected and photographed through a window in the wall of the eye bulbus By increasing the intraocular pressure fr m 15 20 mm a distinct compression of the ciliary vessels became apparent Some cap llaries closed entirely and in some parts the veins were particularly pressu e sensitive The effect on the vessels increased with rising tens n A l scussi n f llowed on the significance this had for the process of tonograj hy an l it was agre l that there is little probability that the rise in tension com ng wh n a t n met r s placed on the eye will not influence the production of aqueous humor

W i l e m a n n J *Tl r ib cyt penia with Dia nox treatment*

A 68 y ar ll w man was eported who had been treated for 6 years with 2 0 mg D m x la ly l e u c f glaucoma She now had symptoms of severe thromboocytopenia. The c n l t n mpr ve l after d scontinuing the D amox Resuming D am x treatment c ulted n w rs i ng f the cond tion which was again improved withdrawing the lrug A u cy w s g i f the usual complications seen under Diamox treatment.

Valebjorg H *Once again on the diagnosis of cataract*

The speaker was against keeping the diagnosis of cataract from the patient as long as possible The patients had to have an explanation for their reduced vision, and if one told them the situation most of them were relieved

Discussion Weidemann suggested that one should get away from the word gronn stær and call it glaucoma as is done in many other countries

Syrdalen Per *Retinal detachment and vitreous bleeding*

In 1967 133 patients with retinal detachment were admitted to the eye department of Rikshospitalet Eleven had already had one vitreous bleeding and another eleven had signs of vitreous bleeding when received in the department altogether sixteen per cent The most probable explanation for these vitreous bleedings was described.

In a case of retinal detachment without vitreous bleeding the time from examination by an ophthalmologist to admission is usually less than one week However if there has first been vitreous bleeding the time is usually several weeks or months The retinal detachment is hidden by these bleedings and the diagnosis is therefore often made very late With heavy vitreous bleeding one should therefore always consider the possibility of a retinal detachment The patient should lie in bed with the head and upper part of the body in an elevated position the patient should preferably use binoculus A good view into the eye is usually obtained within a few days

Discussion *Roe* pointed out the danger of the macula becoming detached if the patients have their retinal detachment too long *Nyquist* mentioned the importance of the patients subjective symptoms giving some idea of the diagnosis even in those cases where the fundus could not be inspected

Kolstad A *Can our pilocarpine drops be improved?*

The pilocarpine drops utilized up to now can be improved since they have a low pH value and contain a mercury preparation not seldom giving an allergic reaction Our pipette bottles are also not good In cooperation with a medical firm the speaker had produced some drops with pH values of 6 5 At this pH the pilocarpine is found to a larger extent as a not dissocciated alkaloid which may increase effectivity Polyvinyl alcohol was added to the drops A mixture of EDTA and benzalconium chloride was utilized as conservant Experience over 2 years showed that the patients felt that these drops were more pleasant to use and on average a somewhat more satisfactory decrease of the intraocular pressure (averaging 3 mm Hg) was obtained

Discussion *Horven* asked about the durability of the drops At 15° C they were stable for three months and at 25° C for one month before a reduction of 10 % was observed It was further discussed whether the present prescription on the pipette bottles that the eye drops should be used within one month after delivery from the chemist was justified The prescription will probably be omitted

Bertelsen T *New investigations into fibrillopathia epitheliocapsularis so called senile exfoliation*

Earlier electron microscopic investigations were recapitulated The amorph layer that is demonstrated basally in the lens capsule in the equatorial zone never has a larger continous extent but is found like islands The speaker was of the opinion that the exfoliation material originated here

Discussion *Petersen* By slit lamp investigation one can find cases where it is only fnokk (i e deposits of Busacca) on the part of the pupillary pigmented edge clo

sest to the iris stroma (i e farthest from the lens) From long term observation it can be seen that these fnokk do not move and consequently may be firmly connected with the pigment. Further deep down between the pigment folds can be found a fine white more diffuse layer that can possibly represent the first tiny formation of the exfoliation material When an enucleated glaucoma eye with exfoliation is examined it is striking how abundant exfoliation material could be spread over the ciliary body and iris and it was not easy to understand how these large amounts of material could be produced by the lens alone Consequently much could be in favour of the exfoliation material being produced in the pigment epithelial layer in the ciliary body and iris *Bertelsen* felt that Petersen *laid too much emphasis on the results of the slit lamp* examinations It was much more common to find exfoliation deposits on iris than the impression given from the slit lamp Examining exfoliation in an autopsy material showed that most exfoliation material was always found on the anterior of the lens It was possible that the exfoliation material could be produced in more than one place but he did not believe so

Odland M *Familial appearance of pigmentary glaucoma*

The characteristic clinical features of this type of glaucoma were mentioned and a family with several cases was reported

Discussion *Petersen* mentioned a ?9 year old man with the typical clinical picture. Heavily pigmented trabecular meshwork After a strong acute rise the tension was normalized and a discussion followed on whether the high tension might have pressed the pigment through the trabecular mechwork and possibly made a sort of dra nage because young people have a more elastic trabecular meshwork *Kolstad* mentioned a patient who got a considerably increased pressure with mydriatics when a large pigment expulsion in the aqueous humor was found The rise in tension was temporary and subsequently the tension remained at lower values than before the experiment.

Flage T *Mooren s ulcer*

A 6? year old man was reported who had symptoms at first in the right eye Here the disease worsened in spite of treatment with excision of the ulcer *margins and later* lamellar keratoplasty By now signs had appeared in the other eye however here it seemed that Prednisolon had stopped the progression.

Discussion *D cisler* reported on a patient with Moorens ulcer in the remaining eye The symptoms started more than 10 years ago and *conservative* treatment and a conjunctival flap were tried without success Then a keratoplasty with auto grafting was performed and the condition remained satisfactory for a long time There was considerable astigmatism but good vision with contact lens Signs of a relapse now appeared *Malling* was of the opinion that the disease was not always on both sides He had followed a case for 0 years *Braathen* said that if the little edge with normal cornea near the limbus is lost the ulcer will never heal *Thomassen* mentioned the doubtful prognosis Neither keratoplasty nor a conjunctival flap will always lead to success Khoe mentioned a case that had been well for six years after lamellar keratoplasty

Hans Walther Larsen Manual and Color Atlas of the Ocular Fundus Copenhagen Munksgaard 1969 Pp 312 523 color pictures Price D kr 400 – $ 55 – £ 23 6 8 – DM 212

This monumental manual and color atlas of the ocular fundus is considered the most elaborate and technically superior presentation hitherto published in its kind

The book consists of two parts the *manual* (p 11 119) with descriptions of the affections of the ocular fundus illustrated in the *atlas* (p 121 301) by 523 color photographs which are accompanied by an explanation and brief clinical notes

This idea of an expansion from the customary limits of an atlas by adding more comprehensive descriptions is certainly a good one and a real engagement at the same time. The author s choice appears optimal regarding the proportions of the manual avoiding the many details belonging to a text book and a unsatisfying too short style He has succeeded in very precise and adequate descriptions comprising general clinical aspects heredity when indicated morphology with differential diagnosis and histopathology References of reasonable dimension are to recent literature from accessible sources

The complete separation between the manual and the atlas involves an alternative study of the two parts with much turn over References facilitates this activity and turn over could not be evaded anyhow To the reader s comfort the manual is printed on mat paper the atlas on excellent coated art paper

Might the author have competitors in description he again appears master in fundus photography His previous Atlas of Diabetic Retinopathy 1959 and Atlas of the Fundus of the Eye 1964 have been of great success and this could but be repeated this time too The fundus pictures are simply superior One explanation must be the author s combined command of ophthalmology and the refined technique of fundus photography

All photographs have been taken by the author with a Zeiss Camera or a Nikon Hand Camera on Agfacolor or Kodachrome Normally the photographs are enlarged 2 5 times the several montage photographs 1 75 times Ordinarily 30° of the fundus is visualised in the pictures but also some originally of 15 are reproduced

The content is rather complete comprising not only common affections in ample variation but also rare lesions are presented The normal fundus is well described Next come congenital variations and disorders affections of the optic nerve and phacomatoses Fundus changes in vascular diseases are well represented as are fundal representations of other systemic affections as blood diseases and metabolic diorders 30 pictures of diabetic retinopathy demonstrate the author s still flourishing interest Further a multitude of degenerative changes inflammatory lesions (posterior uveitis) retinal detachment tumors and injuries

The author s combined efficiency as mentioned obliges the technique and layout involved in the final publishing These are excellent too

The book demonstrates the long art of ophthalmoscopy impressing and pleasing the observing ophthalmologist himself and the whole medical profession as well Recommendation to all interested in ophthalmoscopy or interpretation of fundus observations *P Brændstrup*

Karl Velhagen Der Augenarzt 2nd revised and extended edition Vol 1 with 555 illustrations some in colour Leipzig Georg Thieme 1969 849 pages Price DM 135 –

That was fast work. The 1st edition of "Der Augenarzt" had hardly been completed before the 2nd edition was on its way. Judging by the 1st volume, the second edition is going to be appreciably *larger*, but it is believed that it will not exceed 9 volumes – a complete manual. Possibly the volumes will increase not only *in number* but also *in size*. Vol. 1 of the second edition is 140 pages larger than vol. 1 of the first edition. The basic idea is to be maintained, but the arrangement of the subjects has been somewhat altered.

Vol. 1 contains the following sections: Morphology (J. Rohen), perception of light physiology (Monje), physiological chemistry (Pau and Graeber), pharmacology (Velhagen), general examinations (Velhagen), diagnostic methods (Heydenreich), visual field studies (Schober), *methods of testing perception of light (Comberg and Heydenreich)*, methods of testing colour sense (Heydenreich).

According to random samples, the subjects seem to have been carried entirely up to date, the most recent advances in ophthalmology having been added.

The book has extensive bibliographies, an author index, and a subject index, and its more get-up is excellent and sound.

Holger Ehlers

J. P. H. Alkemade: Dysgenesis mesodermalis of the iris and the cornea (A study of Rieger's syndrome and Peters' anomaly). 206 pages, 73 figures, 6 illustrations in colour, 17 tables. Price Dutch fl. 54.0. Royal Vangorcum Ltd., Assen, The Netherlands 1969.

This monograph, the first on the subject, gives a thorough account of the clinical features, genetics and pathogenesis of these conditions, based partly upon the author's personal experience from 15 cases and partly upon extensive studies of the literature (about 450 references).

The main part of the book presents an exceptionally thorough assessment of Rieger's syndrome, Peters' anomaly and the differential diagnostic possibilities being afforded large space. In the last chapter the author's cases are reported.

An excellent author and subject index as well as a detailed list of references make the contents easily accessible to the reader.

The volume is of very attractive appearance and the illustrations are extremely well chosen and instructive. Unfortunately, a number of printer's errors have slipped into the text.

Finn Kruse Hansen

Course in Retinal Detachment

The Retina Service Massachusetts Eye and Ear Infirmary will sponsor a course in retinal detachment on May 21 22 and 23 1970 The curriculum will include lectures covering the fundamentals of fundus diagnosis pathogenesis and modern methods of treatment of detached retina Tuition is $ 125 for practitioners Residents $ 50 upon application from Department Head Checks are payable to Massachusetts Eye and Ear Infirmary and should be sent to Charles Regan M D Retina Service Massachusetts Eye and Ear Infirmary 243 Charles Street Boston Massachusetts 02114

International Orthoptic Congress

in the International Congress Centre R A I in Amsterdam the Netherlands on 11th 12th and 13th May 1971 The three main themes will be 1) visual acuity 2) the scope of orthoptics 3) squint in disease Any information can be obtained from the Congress Bureau 199 Oudezijds Achterburgwal Amsterdam C the Netherlands

The VIIIth ISCERG Symposium

The VIIIth ISCERG Symposium (International Society for Clinical Electroretinography) will be held in Pisa (Italy) on 7 11 September 1970

The main topics will be

1) Correlation between histology and electrophysiology of the retina (introduced by Prof W K Noell Buffalo U S A)
2) Electrodiagnostic procedures in visual pathology of children (introduced by Docent Birgitta Zetterstrom Stockholm Sweden)

Free papers will also be accepted

Information Prof Dr Alberto Wirth ISCERG Symposium 1970
Clinica Oculistica Universitaria 56100 Pisa (Italy)

Society of Eye Surgeons

The International Eye Foundation is pleased to announce the formation of the Society of Eye Surgeons Its purpose is to promote the science of ophthalmic surgery among all peoples and nations Qualified ocular surgeons may apply for detailed membership information and application forms to J H King Jr M D Director The Society of Eye Surgeons 5255 Loughborough Road N W Washington D C U S A 20016

The Department of Ophthalmology
(Head Prof Dr med Viggo A Jensen)
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ON THE PROGNOSTIC VALUE OF INTRAOCULAR PRESSURE IN TREATMENT OF RETINAL DETACHMENT

BY

NIELS EHLERS and ERIK ØSTERBY

In 45 cases of retinal detachment *Ehlers & Riise* (1967 1969) observed unfavorable results to treatment in cases where the intraocular pressure in the eye with detachment was low or considerably decreased compared with the contralateral eye The object of the present investigation was to further study this correlation in a larger series of patients

The material comprised 155 consecutive cases of retinal detachment admitted to the Department of Ophthalmology Århus Kommunehospital in the period Jan 1 1964 to Dec 31 1968 53 cases were excluded for the following reasons 19 where surgery was not performed (on case of spontaneous healing) 10 where information as to intraocular pressure was not available, 6 with glaucoma and 18 with various intraocular disorders (uveitis perforating lesions epithelial growth in the anterior chamber diabetic retinopathy and phthisis bulbi)

The remaining 102 cases consisted of 63 women with an average age of 57 years (19 [illegible]) and 39 men with an average age of 48 years (11 74) The intraocular pressures were measured by applanation tonometry on the day of admission The results of treatment were judged on the basis of the hospital records The operative procedures employed were diathermia cryoapplication, extrascleral indentation often with Rosengren s silverball or cerclage. The material is presented in Table 1 column 1 In columns 2 and 3 it is divided into 57 cases where reattachment was achieved and 45 where reattachment was not

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achieved These two groups are almost indentical as regards age refraction duration of detachment and number of holes With regard to the extent of the detachment and the operative procedure used, there are more total detachments in the non reattached group and an encircling procedure has often been tried

Table I

	Total 102	Reattached 57	Non reattached 45
Age			
0–20 years	5	1 (2 %)	4 (9 %)
21–40 years	12	8 (14 %)	4 (9 %)
41–60 years	46	27 (47 %)	19 (42 %)
61–80 years	39	21 (37 %)	18 (40 %)
Refraction			
emmetropia + hypermetropia	35	20 (35 %)	15 (33 %)
0–5 D myopia	30	16 (28 %)	14 (31 %)
> 5 D myopia	31	16 (28 %)	15 (33 %)
Afakia	6	5 (9 %)	1 (3 %)
Duration of detachment			
<1 week	31	19 (33 %)	12 (27 %)
1–2 weeks	29	15 (27 %)	14 (31 %)
2–4 weeks	8	4 (7 %)	4 (9 %)
>4 weeks	34	19 (33 %)	15 (33 %)
Number of holes			
0	10	5 (9 %)	5 (11 %)
1	55	33 (58 %)	22 (49 %)
2 or more	37	19 (33 %)	18 (40 %)
Extent of detachment			
1 quadrant	4	4 (7 %)	0 (0 %)
2 quadrants	61	37 (65 %)	24 (53 %)
3 quadrants	23	14 (25 %)	9 (20 %)
4 quadrants	14	2 (3 %)	12 (27 %)
Operation			
Diathermia	29	17 (30 %)	12 (27 %)
Cryopexia	4	4 (7 %)	0 (0 %)
Extrascleral indentation	45	26 (45 %)	19 (42 %)
Encircling procedures	24	10 (18 %)	14 (31 %)

Absolute values for intraocular pressure

Table II shows mean values for intraocular pressure. In the entire series as well as in the two subgroups the mean pressure was significantly lower in the eye with detachment than in the contralateral eye. There are however *no significant differences* in pressure in either *the detachment* eye or the contralateral eye between the reattached and non reattached cases.

The observed pressures are low. *Moritera* (1960) found a pressure of *13.4 ± 0.1 mm Hg in 265 eyes with detachment*. In the present investigation the pressure in the contralateral eye was found to be only 13.3 mm Hg. *This is* lower than the normal intraocular pressure and compared with the findings of *Goldmann* (1957) (15.45 ± 0.13, N = 400) significantly lower. *Yoshioka & Endo* (1966) also state that the ocular tension in the contralateral eye is slightly lower than normal.

Pressure reduction in the detachment eye

In the present material the mean pressure difference of 2.1 ± 0.3 mm Hg was found between the detachment eye and the contralateral eye.

In the group with reattachment a pressure reduction of 1.8 ± 0.4 mm Hg was found, in the group without reattachment 2.5 ± 0.5 mm Hg. The pressure reduction *is thus greatest in the group without reattachment*, but the difference is not statistically significant.

Single measurements of intraocular pressure are encumbered with some uncertainty. Reduced *pressure is therefore in the present study arbitrarily defined* as a difference between the two eyes of more than 2 mm Hg. The material was thereby divided as shown in Table III. Pressure reduction was found in 40 %

Table II

The mean intraocular pressure in mm Hg in eye with detachment and in contralateral eye

	Detachment eye	Contralateral eye
Total	11.2 ± 0.4	13.3 ± 0.3
Reattached	11.8 ± 0.4	13.7 ± 0.4
Non reattached	10.4 ± 0.6	12.9 ± 0.4

The table shows mean ± standard error of mean.

In the literature a pressure reduction is stated as being present in up to 70 % (*Huerkamp* & *Behme* 1955, *Moritera* 1960) a frequency also observed in the present study if a pressure difference of 2 mm is not demanded

Table III shows that reattachment was obtained in 40 (65 %) of 62 cases with the same or higher pressure in the detachment eye In the group with pressure reduction 17 (43 %) reattached cases were found out of 40 The frequency of healing is thus significantly reduced with reduced pressure (χ^2 Yates = 4 06 $P < 0\ 05$)

A higher pressure was measured in the detachment eye in 14 cases in these reattachment was observed in 7 There were 8 cases with disinsertions of which 4 were reattached In 2 cases of disinsertion the highest pressure was in the detachment eye These findings correspond to those in larger series (*Huerkamp* & *Behme* 1955)

Discussion and conclusion

In the present material a poorer result of treatment of retinal detachment was observed when the preoperative intraocular pressure was reduced more than 2 mm Hg As seen from Table I the two groups reattached and non reattached are comparable There are however more cases of total detachment among the non reattached Do these cases have a low pressure and are they responsible for the poor results in the group as a whole? This is true to some degree as 9 of the 12 cases with total detachment and without reattachment had reduced pressure preoperatively Among the remaining 33 cases without reattachment there are however still 42 % with reduced pressure as compared to only 30 %

Table III
Results of treatment of retinal detachment

	Reattached	Non reattached	Total
The same or higher pressure in detachment eye	40	22	62
Reduced pressure in detachment eye	17	23	40
Total	57	45	102

The table shows number of cases

among the reattached cases The two cases of total detachment that did reattach did not have reduced pressure preoperatively *Kleiner* (1933) reported an average pressure reduction of 4 mm Hg in cases of detachment His Table 3 shows that the pressure reduction among the reattached cases was only 2 5 mm Hg All pressures given were measured with a Schiotz tonometer It is not possible on the basis of Kleiner's work to set up a table as Table III in the present paper but among the reattached cases a pressure reduction greather than 2 mm Hg was found in 46 % In the remaining cases where however no direct statement is made that reattachment is not achieved a pressure reduction was found in 60 %

It seems justified to conclude that a relatively lower pressure in the detachment eye is a factor of some prognostic value i e reduced pressure compared with the contralateral eye provides poorer prospects for reattachment

Summary

Among 102 cases of retinal detachment the intraocular pressure was found to be lower in the detachment eye than in the contralateral eye No significant difference was found between pressures in the reattached and non reattached cases There was a significantly lower frequency of reattachment ($P < 0\ 05$) among cases with a pressure reduction of more than 2 mm Hg than among the remaining cases of the material

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LEBER s DISEASE V

BY

TOVE SEEDORFF

SUMMARY

This is the final of a series of papers reporting attempts to elucidate the heredity of Leber s optic neuritis by following descending female lineage in 70 pedigrees described first by Lundsgård in 1944

The present paper deals with 16 families 4 of which have propagated so abundantly that during continued follow up they must be considered of value in studying the mode of inheritance The remaining pedigrees are for various reasons not suited for affording particulars about the inheritance of the carrier property The discussion concerns the possibilities of obtaining an ideal material for determining the carrier rate As the carrier property is disclosed mainly by manifestation of the disease among the descendants the ideal basis for calculation comprises only women who have got so many descendants that there is ample chance of manifestation However the study has shown that only a few families reproduce so briskly as to afford a basis for deciding whether the carrier rate is 50 % or 100 % among the girls born in the female lineage

The conclusion of the whole study is that in the two families with the best reproduction the carrier rate among the women born in the female lineage is higher than 50 % among reproductive women 100 % This seems so clear that it cannot be interpreted as a chance accumulation of carriers The other pedigrees do not include examples militating definitely against this interpretation

100 % carriers among the daughters of carriers and healthy men is not in

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ccordance with Mendelian proportions It is uncertain therefore whether the rait of Leber s disease is chromosomal Thereby it is also uncertain whether his trait may be expected to have same stability as a gene This combined with a wish to see further examples of briskly reproducing families which may confirm the result is the reason why the author does not consider the finding of 100 % carriers among the carriers daughters as being an established general rule for all families with Leber s optic neuritis

Introduction

The following 16 pedigrees will be described more briefly than in the previous papers Information about who first published the individual cases will be omitted This will facilitate the reading to those who do not have access to the original material In more thorough studies however it will make a comparison with Lundsgård studies rather more difficult The method of the study has been described previously and will be supplemented here only by characteristic features of the course of the study Case histories will be given only if they differ from the expected course or if the case has been interpreted temporarily as some other disease of the optic nerve Comments to the individual pedigrees comprise a criticism of the pedigree as a basis for calculation or a criticism of the knowledge concerning the number of manifestations In pedigrees B E F and T examples are adduced which elucidate the criterion of non carrier In the final discussion the present state of the total material is described as a result of a clinical testing of a number of genetic theories which have been summarized previously (Seedorff 1968) It is pointed out that a teamwork by geneticists statisticians pathologists physiologists biochemists neurologists and ophthalmologists is needed to solve the questions still attaching to the disease

Pedigree B

Method

In the first review of the pedigree in 1961 only one new case was found B 131 who had developed the disease already while Lundsgård was preparing her thesis In 19(a new case was reported from the Gentofte Hospital Copenhagen This proved to be B 130 In 19(8 inquiries were sent to a few persons of the 5th and 6th generations and to practically all of the 7th generation The reply rate was fine in Denmark, but no replies were received from U S A. The 19(8 review did not bring to light any further cases

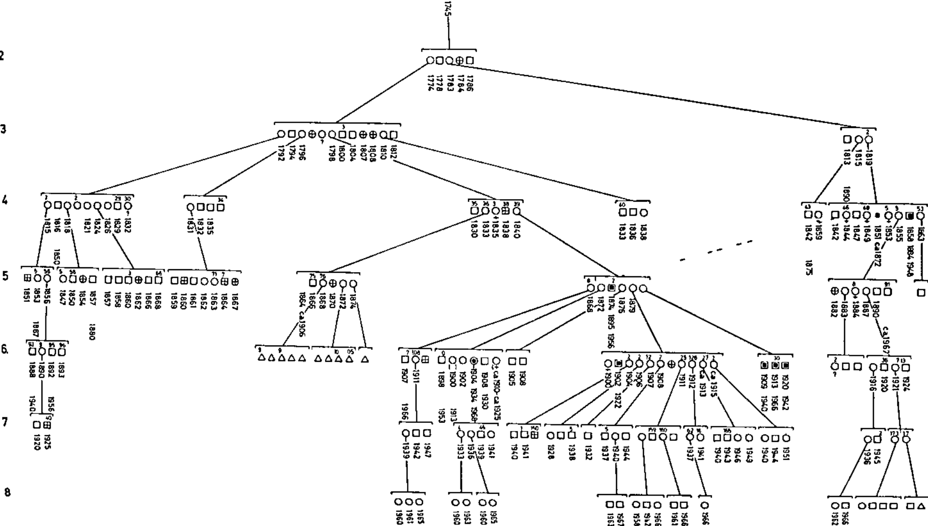


Fig 1
Pedigree B

Results

The pedigree now comprises 192 persons having been supplemented by 55 persons of the youngest generations

Those branches which comprise descendants of B 39 and B 51 have been easiest to follow They include the 2 new patients both of whom have typical histories and both of whom have been admitted to hospital during the developmental stage of the disease

B 130 M J born 30 4 1913 Gentofte Hospital admitted to the Eye Department on 3 10 1966.
B 131 S J born 16 1 1920 Eye Department Rigshospitalet University of Copenhagen (19 1942) admitted on 25 12 1942

Moreover 2 cases of colour blindness were found (B 136 and B 138)

As to the value of the data concerning the unaffected persons

B 90 has been living in Iowa where he ran a farm with his brother It is not known whether he is alive or whether he has good vision.

B 91 also lived in Iowa and as far as is known he had good eyesight until his death around the age of 75 He visited Denmark the year before he died but unfortunately the author did not know he was here.

B 93 has been living in America and nothing is known about him

B 96 answered in 1961 that his eyesight was good and that his brothers had had normal eyesight until they died

B 107 died at 59 years of age very isolated and unfortunately there are no definite data about his sight.

B 110 emigrated to America in his youth He had good eyesight until his death and had always been in close touch with the family in Denmark

B 116 replied in 1961 and 1968 for himself and his brother that both had good eyesight.

B 133 and 134 are presumably living in U S A Nothing is known about them apart from their surnames Their mother and grandmother are living in California

B 136 answered in 1968 that he had good eyesight but was colour blind

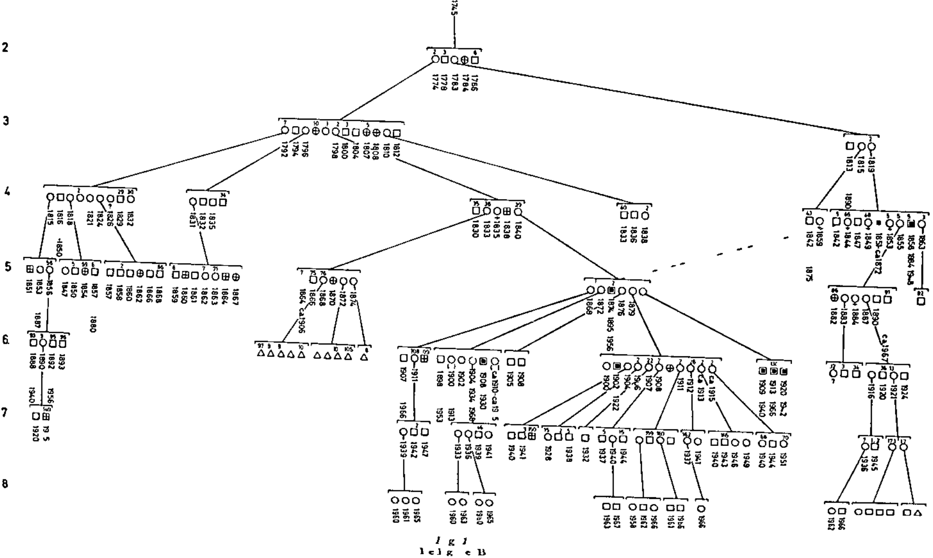
B 138 attended for examination His vision in both eyes was 6/6 he had no scotoma for white 3/1000 but was entirely red green blind when tested with Ishi Hara s plates

Among the descendants of B 84 migraine is considered a familial weakness affecting many The study did not include the frequency of migraine but spontaneously it has been stated that B 120 B 126 B 127 B 157 and B 162 are sufferers and presumably there are others

The following factors reduce the value of the pedigree

Among the descendants of B 7 there are two contemporary persons B 36 and B 139 both healthy Unfortunately they do not know the name of B 7 and thus cannot confirm that the study is on the right track Only manifestation of the disease will be able to confirm this Nevertheless if B 139 reaches the age of 60 without developing the disease it must be considered reasonable to designate B 7 as non carrier

The complete data of the christening og B 57 73 are available These persons were born in Southern Jutland during the interval between the two Dano German wars in 1848 and 1864 but their fate is unknown presumably as a consequence of the moving of the frontier Complete christening data have also been found for B 74 79 and mar



the predisposed persons gradually as they become 60 in the eye department closest to their homes

Pedigree E

Results

This pedigree now comprises 64 persons 25 women and 39 men It has been supplemented by 5 persons of the youngest generation. One new case has been found and thereby a new carrier has been demonstrated The new patient is

E 45 H H L L born 19 7 1905 This patient has been in the Mental Hospital Mid delfart for a number of years with schizophrenia His eyesight was considered normal by his family as well as by the hospital staff because his orientation in the ward was normal On occasion of the present study he was examined in 1965 by the hospital ophthalmologist who found bilateral atrophy of the discs normal pupillary reactions and normal tension His mental state excluded any collaboration on his part so that it was not possible to determine vision and visual field. Nor could he state his own opinion of his eyesight

Comments Although the developmental stage of the disease was not observed and cannot be dated the familial predisposition makes Leber s disease the most likely diagnosis

Re value of symbols for healthy males

The males of the sibship in the 2nd generation were born in Schleswig Holstein Possibly they have lived in Copenhagen for some time but later moved to Germany Therefore we have no data about their vision The carrier E 6 was born in Copenhagen and married a Danish citizen. Her sons the men of the 3rd generation emigrated and died in Germany Havana Glasgow and Australia respectively Accordingly noth ng is known about the v sion of E 8 9 and 13 F 12 who was a grocer in Glasgow visited Denmark in 1877 and on this occasion consulted an ophthalmologist Therefore we know that he was suffering from the disease It is not until the 4th generation that the symbols for healthy male are reliable

There are 8 manifestations of the disease in the pedigree The 4th generation is ready for calculation The disease has been recorded in

26 % of the boys born in the 4th generation (5 out of 19)

38 % of the boys who lived to be 10 (5 out of 13)

44 % of the men who lived to be 60 (4 out of 9)

There are 6 carriers in the pedigree The 3rd generation may be counted Out of a total of 4 women one was undeterminable and 3 were carriers

The 3 carriers have had a total of 9 daughters 5 of whom were undeterminable 2 carriers and 2 are under observation In other words more than half the women of the generation under observation are undeterminable

Col ur bl n lness is p esent in this pedigree E 12 and E 25 have reported that they were colour blind before they developed Leber s disease According to information from their next of kin E 35 and E 41 were also colour blind and E 56 states that he i colour bl nd

riage data for B 76 and 78 but unfortunately the knowledge that Lundsgård had of the offspring of B 76 78 and 79 has been lost

Among the sibship B 45 53 the females B 50 51 and 53 emigrated to USA B 51 went in 1890 leaving one of her children the daughter B 89 in Denmark. Therefore, B 89 and her descendrants are Danish while the remaining of the listed descendants of B 51 and B 53 are living or have been living in USA The names and addresses of a number of the family members in USA are known but they have not replied in quiries

B 56 and B 83 now have each 2 male descendants who have reached the age of 60 without having developed the disease It must be reasonable therefore, to consider them non carriers

Comments

There is nothing in pedigree B to militate against Leber s disease being inherited according to Mendelian proportions But owing to its incompleteness and the consanguineous marriage of B 39 and B 45 this pedigree does not give satisfactory information about the mode of inheritance of Leber s disease Its main value is that the descendants of B 84 afford a good observation material If manifestations appear among them this will occur within the next few years The fact that the women of this branch suffer from migraine which perhaps bears an unknown relation to Leber s disease lends further interest to this observation material

How the two cases of colour blindness have entered the family cannot be decided on the basis of the data at hand There is no information concerning colour blindness among the ancestors

This is the first time the material presents women who are by way of being considered non carriers – It was the experience from pedigree A which gave rise to a presumption that a criterion of non carriers could be set up The 5th and 6th generations of pedigree A include boys in 11 sibships In 10 of these sibships the eldest son is affected while the eldest son of the 11th sibship is healthy Thus at the completion of studying pedigree A it seemed reasonable to consider a woman as non carrier when her two oldest male descendants have reached the age of 60 without developing the disease However examples from pedigrees E Γ and T show that this criterion does not hold as the woman may be a carrier nevertheless Therefore the criterion of non carrier is uncertain Unfortunately the fact is that the more male descendants are demanded before a woman is declared non carrier the more undeterminable women will be found in the pedigrees It was considered to introduce a special symbol for a woman having two 60 year old male descendants with good vision to keep an eye on such women in particular Regrettably the persons in question have not been examined by an ophthalmologist and therefore this symbol has not yet been introduced In the future this drawback may be remedied by examining

the predisposed persons gradually as they become 60 in the eye department closest to their homes

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Colour blindness is present in this pedigree E 17 and E 25 have reported that they were colour blind before they developed Leber s disease According to information from their next of kin E 35 and E 41 were also colour blind and E 56 states that he is colour blind

Fig 2
Pedigree E

The colour blindness has entered the family through the progenitor E I s husband He had come to Copenhagen from Schleswig Holstein because he had been the queen s physician in ordinary from her youth and he became professor to the University of Copenhagen He corresponded with Goethe and on occasion of Goethe s Farbenlehre he wrote him a letter in 1811 which Goethe published In this letter he described his impression of the colours of silk of the sky flowers minerals and jewels paintings oleum ricini and of the patients skin In his own opinion he was suffering from violet blindness akyanoblepsie but he wrote among other things that the redness of the sky was merely a thing he knew from reading and that he was unable to distinguish white silver ore from red Thus his colour blindness might also have been red blindness

Violet blindness is so rare that the family would be worth a further study At the same time the male lines could be reviewed for Leber s disease Therefore the persons of the male lineage are recorded 48 persons including the 14 from the pure female

lineage were born in the *5th generation* of pedigree E during the period 1899 to about 1930 For the time being this material has been put aside

Comments

Three carriers in one sibship may be a chance accumulation. The high incidence of carriers must repeat itself in the subsequent generations before the pedigree can afford the desired information concerning the mode of inheritance

E 11 was found to be a carrier in 1936 when her eldest daughter s son developed the disease She herself had 4 sons who were healthy including 2 who had lived to be about 75 Had E 11 not had this daughter she might have been taken to be non carrier

Pedigree F

Results

This pedigree now comprises 93 persons 37 males 54 females and 2 of un known sex It has been increased by 44 persons One new case has been found in the youngest generation and this disclosed 3 carriers

Eldest son of F 62 A. F P born 24 4 1943 Dept. of Neurosurgery Rigshospitalet Uni versity of Copenhagen 363/0/1965 admitted 6 12 21 12 1965

In September 1965 the patient had noticed blurring before the left eye and one week later also before the right eye Examination at the Central Hospital Næstved in No vember 1965 showed the vision in the right eye to be 3/60 and in the left eye finger counting at a distance of 0 5 m Ophthalmoscopy Pale disc on the left. Visual field Outer limits normal EEG Suspicion of a focal lesion in the right occipital lobe Ac cordingly he was transferred to Rigshospitalet, Department of Neurosurgery and on 8 12 1965 he was examined in the Eye Department Rigshospitalet, Tagensvej Vision in right eye 6/40 in left eye finger counting at a distance of 10 cm Visual field of right eye Quadrant c anopsia superotemporally central scotoma of 10° In addition, endocrine signs such as decreasing libido and weight gain There was thus indication for exploratory craniotomy with a view to a tumour in the region of the chiasm. At operation the optic nerves were found to be slightly injected perhaps somewhat thin ner than usual but not definitely abnormal Arachnoid adhesion was found below and anterior to the chiasm After the operation the vision in the right eye was 1/30 and in the left eye finger counting Diagnosis Bilateral optic neuritis The patient was then referred to the State Institute for the Blind and Weaksighted where by chance he was examined by the present author Since at that time pedigree F had been studied h s relationsh p to family F could soon be disclosed The patient himself was unaware of the predisposition The correspondence had been with his maternal grandmother 3 years previously

The following data will be given to elucidate the value of the symbols for healthy male among the descendants of F 14

Ac rding to information from their sister F 33 F 30 31 and 34 had good eye s ght until they died at 0 or older F 45 had good eyesight at 60 according to his

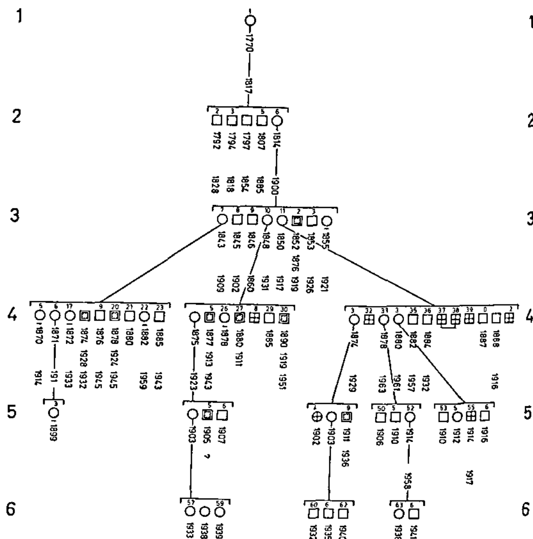


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Violet blindness is so rare that the family would be worth a further study At the same time the male lines could be reviewed for Leber s disease Therefore the persons of the male lineage are recorded 48 persons including the 14 from the pure female

sister F 44 and this same sister stated that F 5? 54 and 55 have good vision in 1969 – *now aged 67 64 and 60*

The pedigree includes 8 carriers (3 of whom were also affected) The 4th generation is ready for calculation of the carrier rate Among descendants of F 14 5 girls had been born 2 of whom were undeterminable and 3 carriers (one of whom was affected as well) The 3 carriers have a total of 7 daughters 1 of whom are undeterminable and 3 carriers (including 2 affected) and 3 are under observation Thus in the 5th generation the incidence of undeterminable may get as low as 1 7

Comments
3 carriers in the sibship F 27 – F 34 may be a chance accumulation A high carrier rate must manifest itself also *in the subsequent generations to be convincing*

F 33 was considered non carrier until 1966 At that time she had 2 sons who had reached the age of 60 without developing the disease And then the disease manifested itself in the eldest son of her eldest daughter s eldest daughter Later a third of her sons has reached the age of 60 without developing the disease Thus the criterion of non carrier must be more exacting than first assumed and will thereby become so strict with a view to the demanded number of descendants that it can hardly be fulfilled with the size of the present day Danish families

Pedigree H

Results
This pedigree has been augmented by 7 persons of the youngest generations No new cases have been found In the 6th generation there are two brothers H 31 and H 32 who have reached an age over 60 and who are listed as unaffected The elder one H 31 emigrated to America in his youth and none of the living members has any news of him H 32 stated in a letter in 1964 that his eyesight was good All other men of this pedigree were younger than 60 when the study was closed

H 21 is the oldest carrier and she is the progenitress of that part of the pedigree which is of any importance As to the older persons of this pedigree it *it known only that they have existed* not whether or not they were affected

Comments
With 4 carriers pedigree H is too small to afford any particulars concerning the mode of inheritance but the younger generations make up quite a good material for observation

Fig 3
Pedigree F

Comments

The pedigree includes only 3 carriers viz the mother maternal grandmother and great grandmother of 2 probands Such a pedigree cannot elucidate the mode of inheriting the carrier property

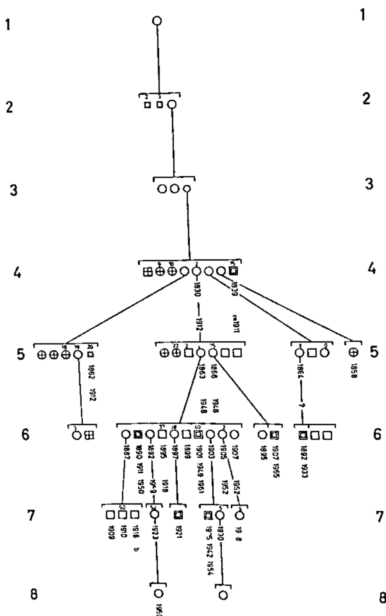
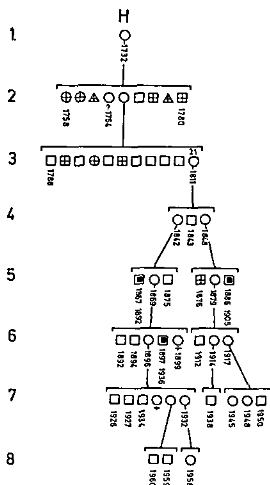


Fig 5
Pedigree K.



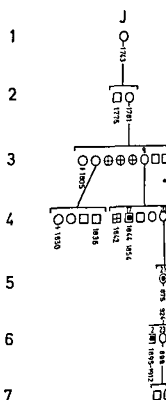


Fig 4
Pedigree H and J

Pedigree J

Results

This pedigree is unchanged since the study of Ruth Lundsgård J 22 cannot be traced J 23 lived in Canada already when Lundsgård was performing her study and her sons are presumably living there too J 24 emigrated to Canada in 1957 Thereby the possibilities of finding living members of the family in Denmark have been exhausted Not much is known about the men listed as unaffected in the 4th generation as they had died before Lundsgård s study According to Lundsgard J 15 must have had some eye trouble because he was said to have always worn dark glasses For J 18 the observation period was only 20 years since at that age he was blinded by an explosion accident

J 9 is the progenitress of that part of the pedigree which is of any importance

K 51 C A J J *born* 31 8 1916 Odense County and City Hospital Dept of Neurosurgery case rec 5 0/1960 61 Admitted as an emergency to the Neurological Dept on 24 10 1960 with right sided hemiparesis At admission his next of kin reported a family history of an eye disease causing blindness *appearing at the age of 30 50 Oph*thalmoscopy Discs well defined well vascularized non congested Visual field Presumably right sided hemianopsia Right pupil larger than the left Bilateral carotid angiography and left sided vertebral angiography Obstruction in the left int carotid artery but not suggestive of thrombosis On 26 10 the patient was transferred to the *Dept of Neurosurgery with severe right sided* hemiparesis pharyngeal paresis and total aphasia Diagnosis Occlusion (kink) of left internal carotid artery 44 453 The case was likened to one described by Qu ttlebaum in 1959 On 29 10 resection of the left int carotid art Control X ray on 2? 11 however showed total obstruction *at the* site of resection On 7 1? exploration at the site The lumen distally to the site of operation was filled with organized thrombotic masses It proved impossible to re establish the flow through the vessel

In February 1965 the author visited the patient on occasion of the present study He *was in a nursing home ambulatory and able to feed himself* He was friendly and co operative apparently understood the object of the visit but was severely aphatic being able to utter only yes and no and count to three Vision Questionable perception of light Ophthalmoscopy Total atrophy of the discs on both sides

Comments It is not known when the atrophy of the discs set in presumably during the m nths after discharge from hospital The severe optic atrophy cannot be explained solely by the carotid thrombosis and it is also not characteristic of Leber s disease As a questionable case this patient is labelled by the symbol for unaffected male

When considering this matter with *regard to his mother* K 34 *she* is among the whole family the only woman with male descendants to be a non carrier Accordingly t is very difficult to defend the view that her son s disease has no relation to Leber s d sease *Another* 2 sons had good vision in 1965 They have now almost reached the age of 60 and then there will be an indication for a repeated examination

This pedigree includes 8 carriers K 7 being the oldest

The 4th generation is ready for calculation 6 women were born 4 of whom are undeterminable and 2 carriers

The 5th generation is also ready now 11 women were born 8 of whom are undeterminable while 3 are carriers

The 6th generation is under observation 8 women have been born 3 of whom are undeterminable 2 are carriers and 3 are under observation

Comments

Owing to the large number of undeterminable women reserve has to be displayed in advancing any conclusions

Pedigree L

Results

This pedigree has been supplemented by a sibship in the 4th generation but

Results

This pedigree now comprises 58 persons 35 females and 23 males It has been increased by 3 persons Before K 54 Lundsgard had listed a person who has now been deleted Three new cases of Leber s disease have been found apart from one case of bilateral optic nerve atrophy due to another cause

K 40 R G F N born 28 1 1901 Admitted to the Eye Department of the St Joseph Hospital Odense from 5 12 1949 to 21 1 1950 The visual impairment had started in the left eye in Oct 1949 in the right eye a few days before admission The course was typical and the patient was aware of the familial predisposition at admission

K 45 A C M A born 22 4 1907 Admitted to the Eye Department of the Arhus Municipal Hospital (8538/65) from 18 3 to 30 3 1965 The visual impairment had started in Jan 1965 in both eyes and the patient was admitted when he could no longer read One year previously he had had nerves because of overstrain In respect to possible poisoning it was known that in the autumn of 1964 he had worked one day on melting lead He reported smoking 3 packs of cigarettes a week and drinking 6 7 pints of beer and a couple of gins a day Since last New Year he had been slimming and had lost 10 kg In addition during the past few months there had been tingling and a sensation of cold in the two ulnar fingers especially on the right Ophthalmoscopy revealed signs of optic neuritis and examination of the visual field showed a central scotoma for white On the basis of the history and because the patient was almost 57 years of age i e had reached an age at which manifestation of Leber s disease is generally not expected the condition was diagnosed as tobacco alcohol amplyopia

In April of the same year the author visited the patient on occasion of the present study and realized that he was affected with Leber s disease

Comments Knowledge of a predisposition makes the diagnosis Leber s disease more likely than tobacco amblyopia As a matter of fact the patogenesis is still so obscure that you can just as well choose the viewpoint the causes perhaps have been collaborating

K 53 C W W born 16 9 1921 Admitted to the Eye Department of the Odense County and City Hospital 5 10–12 10 1953 The patient was aware of the familial predisposition at admission Vision had been deteriorating in the left eye during the past months and he was admitted when the right eye became involved The signs and course were typical

Re symbols for healthy male

In the 5th generation there are 5 men 3 of whom K 20 K 27 and K 29 emigrated to U S A According to Lundsgard K 20 developed an eye disease at the age of 50 K 27 was a farmer and minor business man in Utah while nothing is known of K 29 K 23 was originally a baker but later worked in a biscuit factory died at 74 K 26 was originally a weaver but later became caretaker died at 90 In other words the change of occupation by the latter two at a fairly advanced age might be explained by a visual loss However in 1965 a son of their sister s stated that both had had good eyesight until they died In the 6th generation there are 4 symbols for unaffected male K 37 who died young K 59 who was examined in 1965 and had good vision and lastly K 47 and K 48 about whom nothing is known

K 51 occupies an exceptional position since at the age of 44 he developed bilateral total atrophy of the optic nerve of a complicated genesis

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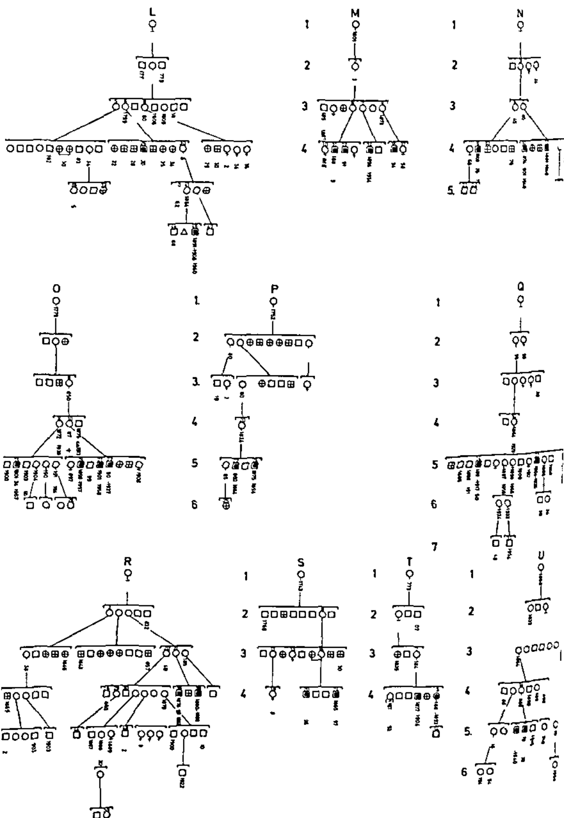


Fig 6
Pedigree L M N O P Q R S T and U

could not be supplemented by any contemporary persons and no new cases of Leber s disease have been detected Much genealogical work has been done unsuccessfully to trace contemporary persons but the knowledge of the sibships L 13 22 and L 31 35 is still restricted to christening data and the knowledge that Lundsgård had of the sibship L 36 39 has now been lost The disease has been demonstrated only among the descendants of L 6 and among them the female lineage is now extinct half her descendants having died in childhood L 44 answered an inquiry in 1965 to the effect that he and his male cousin L 47 also still alive had good eyesight

Comments

In pedigree L there is nothing to militate against the carrier property being transmitted in Mendelian proportions

Pedigree M

Results

It has not proved possible to get into touch with any person of pedigree M The pedigree has not been supplemented and no new cases of Leber s disease have been detected

The code data recorded by Lundsgård were not sufficient to trace the records The code data for M 14 referred to the New York Eye and Ear Infirmary which has not been asked M 16 s address could be traced until 1936 M 10 M 13 M 15 and M 17 are entirely unknown The descendants of M 13 had been lost trace of even before Lundsgård s study

Comments

This pedigree was finished in 1944 As there is only one proband it is fairly valuable The 3rd generation may be included in the calculations Of the 6 girls born in the 3rd generation 3 have had children and all have proved to be carriers However this is too uncertain a basis for altering the views on the laws of inheritance

Pedigree N

Results

All 3 patients of this pedigree had died before the present study war started It has not been possible to supplement the pedigree and no new cases have been detected

Nothing is known about the 2 brothers of the youngest generation Their mother married in Germany and presumably all three have remained German. There are 3 carriers in the pedigree a mother and her 2 daughters 5 women have been born in the 4th generation all undeterminable

Comments
This pedigree is unsuited for assessing the mode of inheritance of the carrier property

Pedigree O

Results
The pedigree has been supplemented by 4 persons of the youngest generation and 2 new cases of the disease have been detected

O 19 H V F H (B) born 11 7 1898 Admitted to the Eye Department of the Copenhagen City Hospital (413/1955) 20 5 14 6 1955
The visual impairment had set in 5 weeks before admission Vision in right eye 6/12 in left eye 1 2/60 Visual field Relative central scotoma for red of 10° on the right absolute central scotoma of 20° on the left Ophthalmoscopy Normal findings Pneumoventriculography showed a small questionable impression into the anterior wall of the 3rd ventricle On 18 7 1955 therefore the patient was transferred for craniotomy to the Department of Neurosurgery Bispebjerg Hospital Operation showed a slightly thickened but not definitely abnormal arachnoid around the chiasmal cistern The optic nerves and chiasm were not involved but the optic nerves were somewhat whiter than normal
Comments The pneumoventriculographic appearances afforded the indication for operation As is apparent from Lundsgård s thesis there was a similar change in the anterior wall of the 3rd ventricle in O 22 (Case 89) who developed the disease in 1934 and arrived for craniotomy at Rigshospitalet University of Copenhagen in 1935
O 21 A A S H born 9 9 01 57 years old waiter since 1930 suffering from anosmia after a cranial fracture since 1940 from hypacusis after otitis Jan 1958 he got a blow of a fist on the back of the head 14 days later visual impairment started in the right eye 1 2 58 he was seen in the Eye Department in Næstved from where he was referred to the Military Hospital Copenhagen 12 3 58 Vision right eye 2/60 left eye 6 6 c corr Field of vision upper bitemporal quadrantanopsia involving right centre Ophthalmoscopy swelling of the discs with slight protrusion blurring of the margins dilated veins and hemorrhages at the margins At this moment symptoms seemed to show intracranial pressure but the history of the family was wellknown 21 3 hemorrhages and venous stasis had disappeared leaving only a blurring of the disc margins and the diagnosis of Leber s disease was accepted Neurological examination was performed but the record could not be found Vision each eye in oct about 1/60 exc fix

This pedigree includes only 3 carriers In the 5th generation there are 6 women 3 of whom are undeterminable and 3 under observation

Comments

The pedigree is still too small to afford any contribution to a conclusion concerning the mode of inheritance

Pedigree P

This is an old pedigree The youngest patient was born 85 years before the present study was started The 2 patients have not been traced and the pedigree cannot be supplemented It includes only one carrier and is too small to give any information about the mode of inheritance

Pedigree Q

Results

Supplemented by 2 persons of the youngest generation One case has appeared

Q 25 A V J born 19 6 1911 This patient had spent 3 years in a German concentration camp The visual impairment started in 1946 and on 16 10 1948 the patient was examined in the State Institute for the Blind and Weaksighted It is apparent from the records of this Institute that he had first been admitted o the Århus Municipal Hospital and to the Neurological Department of Rigshospitalet, University of Copenhagen where his condition was diagnosed as bilateral retrobulbar neuritis disseminated sclerosis and nervousness due to imprisonment At the Institute for the Blind and Weaksighted the family was well known and here the disease was diagnosed as Leber s disease

There is only one carrier in this pedigree Among her 6 daughters 4 are undeterminable while 2 are still under observation

Comments

The pedigree is too small to give any information about the mode of inheritance

Pedigree R

Results

Pedigree R is a large one built up around two patients and their mother who is the only carrier of the pedigree The patients born in 1876 and 1880 had no doubt died before the present study was started It has not proved possible to supplement the pedigree and it is entirely unchanged since Lundsgård s publication Knowledge of R 1 and R 4 and of the descendants of R 3 has been re established but is based exclusively upon archive studies Lundsgård also

knew of the descendants of R 2 through archive studies and moreover she had among the descendants of R 20 such substantial knowledge of the persons living around 1940 that she considered R 20 to be a non carrier R 20 and her descendants have now been completely lost to follow up

Comments
In her chapter on mutations Lundsgård interpreted R 21 as the woman in whom a mutation had arisen stating that the gene disappeared already within one generation because the progenitress (R 21) did not have daughters

The questions whether R 4 already was a carrier and R 20 thus was a healthy daughter of a carrier and whether R 20 was in fact a non carrier cannot be further elucidated and the pedigree cannot be supplemented unless new patients crop up

Pedigree S

Pedigree S is an old one dealing with two brothers who developed Leber s disease before the turn of the century and who must have died long before the present study was undertaken This pedigree has only one carrier It has proved impossible to find descendants of her sisters No information is to be had concerning the mode of inheritance

Pedigree T

Pedigree T is also an old one with one carrier and two patients The latter of these two cases occurred 55 years before the present study was started and neither patient could be traced The female lineage is extinct and the pedigree is unchanged since Lundsgård s study

Comments
The distribution of manifestations in sibship T 8 – 13 is very unusual The three eldest children are healthy the two sons even had good eyesight until they died at a ripe old age If T 7 had belonged to a larger pedigree and if she had had only the three eldest children she might have been interpreted as a non carrier However her youngest daughter developed Leber s disease at the age of only $11^1/_2$ years

Pedigree U

Results

The pedigree has been augmented by 3 persons of the youngest generation all females No new cases have manifested themselves and thus the pedigree still contains only 2 patients and one carrier

Comments

In its present shape this pedigree tells us nothing in respect to the mode of in heritance of Leber s disease

Size of the Total Material

The entire material was entered on a card index system This card index com prises persons whose accurate birth date is known Children who died before the age of 10 were excluded The index gives the actual figures relating to the size of the material i e the number of persons identified by complete data It is not applicable direct as a basis of calculations regarding the mode of inheritance because it includes everybody also persons whose fate is unknown and branches of the families that can no longer be traced

The birthday index was used as a basis of Fig 7 which affords information about the total size of the material and the number of patients It will be seen that each year about 2 3 females and 2 3 males have been born

Annual Number of Manifestations

In Fig 8 the times of manifestations are tabulated to show how many mani festations occur annually Since 1890 up to 2 manifestations have occurred each year

Empirically however more than two cases of the disease arise annually in Denmark and thus there appear to be other families with optic neuritis than those included in this study Concurrently with the present study the author has investigated because of reports of new cases 5 families with sporadic cases of the disease and 10 families in which the disease appears to have developed in only one isolated case In other words since 1960 a larger number of no tified cases have proved to have no connection with Lundsgård s pedigrees than those appearing in the families The files of the University Institute of Human Genetics Copenhagen also include a number of reports on cases from the pe

knew of the descendants of R 2 through archive studies and moreover she had among the descendants of R 20 such substantial knowledge of the persons living around 1940 that she considered R 20 to be a non carrier R 20 and her descendants have now been completely lost to follow up

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	Males			Females		
	Manifestations among persons born after 1870	Manifestations among persons born before 1870	Sum of manifestations	Manifestations among persons born after 1870	Manifestations among persons born before 1870	Sum of manifestations
1860–69		3	3		2	2
1870–79		3	3			
1880–89		8	8			
1890–99	7	6	13			
1900–09	7		7	3	1	4
1910–19	12	3	15	1		1
1920–29	10	1	11	4		4
1930–39	22		22	2		2
1940–49	8		8	5		5
1950–59	16		16	1		1
1960	11		11	1		1
m	93			17		

Fig 8

Times of manifestation

Material divided into ? groups according to whether the persons were born before or after 18 0 The times of manifestation are collected in decades The object of this table is to find how many manifestations occur annually The purpose of considering patients born after 18 0 separately is to make it possible to compare with Fig , It will be seen that 12 24 cases have occurred in each decade since 1910 i e one or two manifesta tions a year The sum 12 of the last decade however is no doubt too low as the study of several of the pedigrees was closed as early as 1964

2 times of manifestation are lacking as the time of manifestation in two males is not sufficiently well known to be placed in a 10 year group

gård a son of the proband s sister became blind in 1939 but the cause of his blindness is unknown as he was living in New York. At present the material comprises only 3 men born after 1915 but presumably this is sufficient for a decision to be made when the time comes as to whether or not an inherited predisposition exists in this family

Fig 40 The list of persons was partially reconstructed and supplemented by , persons 6 of whom were born after 1940 One new case occurred in 1943 in the proband s youngest sister This case was mentioned by Lundsgård in a foot note The pedigree comprises 13 persons born after 1919 still under observa tion

Fig 41 The list of persons in the two youngest generations has been recon

	Males		Females	
	Observed	Affected	Observed	Affected
1860-69				
1870-79	12	10	21	4
1880-89	22	14	19	1
1890-99	39	21	33	6
1900-09	34	18	30	2
1910-19	36	14	35	4
1920-29	31	9	24	
1930-39	26	4	27	
1940-49	35	4	26	
1950-9	28	1	19	
sum	263	95	234	17

Fig 7

Number of persons born during each 10 year period The reason why those born prior to 1870 have been omitted is that non affected persons from these years were estimated not to be fully represented in the register It will be seen that among the persons born in the period 1870 1910 more than half the males have by now become affected Among the younger persons the affected persons as yet make up only a smaller proportion

riod before 1960 which are unrelated to Lundsgard s pedigrees Cf also the following section on Lundsgård s "isolated cases

› Isolated Cases ‹ from the 1944 Study

Lundsgard s paper included another 7 pedigrees depicted in her thesis as Figs 39 45 These pedigrees will be mentioned in outline below without the detailed graphs

Fig 39 The list of persons has been reconstructed but the family has grown by only one boy born in 1953 With the exception of the line from one woman born in 1917 who could not be traced it has been found that the female lineage will become extinct There is a great preponderance of undeterminable women in the generation under observation and the pedigree can give no con clusive answer to the question regarding the carrier rate According to Lunds

	Males			Females		
	M[illegible] among persons born [illegible] 1870	M[illegible] among persons born before 1870	Sum	M[illegible] among persons born [illegible] 1870	M[illegible] among persons born before 1870	Sum
1860 – 69		3	3		2	2
1870 – 79		3	3			
1880 – 89		8	8			
1890 – 99	7	6	13			
1900 – 09	7		7	3	1	4
1910 – 19	12	3	15	1		1
1920 – 29	10	1	11	4		4
1930 – 39	22		22	2		2
1940 – 49	8		8	5		5
1950 – 59	16		16	1		1
1960	11		11	1		1
m	93			17		

Fig 8

Times of manifestation

Material divided into ? groups according to whether the persons were born before or after 18 0 The times of manifestation are collected in decades The object of this table is to find how many manifestations occur annually The purpose of considering patients born after 18 0 separately is to make it possible to compare with Fig / It will be seen that 1? 4 cases have occurred in each decade since 1910 i e one or two manifesta tions a year The sum 1? of the last decade however is no doubt too low as the study of se eral of the pedigrees was closed as early as 1964

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gård a son of the proband s sister became blind in 1939 but the cause of his blindness is unknown as he was living in New York At present the material comprises only 3 men born after 1915 but presumably this is sufficient for a decision to be made when the time comes as to whether or not an inherited predisposition exists in this family

Fig 40 The list of persons was partially reconstructed and supplemented by persons 6 of whom were born after 1940 One new case occurred in 1943 in the proband s youngest sister This case was mentioned by Lundsgård in a foot note The pedigree comprises 13 persons born after 1919 still under observa tion

Fig 41 The list of persons in the two youngest generations has been recon

structed without new cases being found There have been 7 male and 10 female cousins of the proband s two of the males and one of the females living in America As far as may be gathered from talks with a few of the family members all are healthy but the family is far from having been thoroughly investigated Its members are very scattered In particular the emigration to America has had an inhibitory effect upon the initiative for investigation

Fig 42 This is an old pedigree The proband was born in 1838 Lundsgård s knowledge of the family was based merely on studies of archives and she never traced the connection to the present times Nothing has been done to renew the knowledge of this family

Fig 43 The proband cannot be identified and to day the persons are entirely unknown

Fig 44 The list of persons is known from an accidental remnant of Lundsgård s notes The only female line is extinct and this pedigree will never show more than it did in 1944

Fig 45 The pedigree has been supplemented by 28 persons so that now it comprises 52 31 of whom were born after 1900 There are 2 cases of optic atrophy among the male cousins of the proband s Considering the predisposition it is most likely that these are cases of Leber s disease The diagnosis is *in one of the cases Episodic psychosis in oligophrenia history* of alcoholic abuse toxic atrophy of both optic nerves The disease arose in 1957, within one month after a bottle party on a ship in the docks accordingly his neuritis was interpreted as being toxic The other cousin was admitted in 1958 to an eye department as a case of bilateral retrobulbar neuritis Owing to a suspicion of suprasellar meningioma exploratory craniotomy was performed It showed a whitish thickened arachnoid and yellowish optic nerves with a striking number of vessels above as well as below the chiasm but no meningioma These patients next of kin have refused to supply information about the family stating that the causes of blindness were alcohol abuse and brain disease respectively Therefore a study of this family is not really in progress but it would afford a good material for observation

Comments

The carrier rate in these pedigrees is at present no higher than 50 % The pedigrees containing isolated cases show like the rest of the study how families die out due to lacking reproduction in the female lineage but they also give examples of how a case which has once seemed isolated is no longer isolated as time goes on The last pedigree is of most interest showing how one case in a family is so typical that it gives rise to a genetic study while the next two in the same family may *show a rather complicated disease pattern* and do not give any impulse for genetic study

Pedigrees A and C have become ideal The women may be counted in two consecutive generations and in the next generations mothers are so numerous that a result may be expected when the next counting among women can be done Pedigrees B E, F and H also fan out affording observation material but various factors reduce their value Knowledge of family B is reduced by emigrations and by three alterations of the Danish German frontier since 1948 In pedigrees E F and H only one generation of women is really suited for counting and the next generation now under observation (the 5th generation) comprises only 5 6 and 2 mothers respectively Pedigrees D and K include a relatively large number of childless women so that the youngest generations contain too few mothers for elucidating the mode of inheritance The remainder of the pedigrees are characterized by female lines which are small or about to die out and by emigrations which obliterate the trace of the last persons that might be observed

Within this heterogenous material the findings in the ideal pedigrees A and C have maintained the presumption that the daughters of all carriers are carriers themselves because all mothers who have borne so many children that the inherited trait has had a possibility of manifesting itself have proved to be carriers The question is then whether it is justified on this basis to feel convinced that the same applies to all families with Leber s disease

The results of studying the other 18 pedigrees cannot disprove the presumption that all daughters of carriers are carriers themselves as the material does not contain women who can be labelled with certainty as *non carriers* The existence of other families in which the disease occurs more scattered warns against drawing a general conclusion now although these families have been observed for only a short time The fact that the Dutch material includes healthy branches should also urge to reserve. In my opinion therefore it is reasonable to demand a longer observation period so that new generations of satisfactorily observed mothers may be counted before general conclusions are drawn

Considering that a number of the pedigrees embrace 7 generations and that the material includes cases occurring before Leber described the disease in 1871 it may seem surprising that there is still reason to demand a longer observation period to answer the question concerning the carrier rate The question relating to the causes of lacking *reproduction* is incorporated in that relating to the carrier rate and is equally *difficult* to answer Furthermore the observation makes the women aware of the indication for birth control and thereby observation might render it the *more* difficult to attain a result the more efforts are made to attain it

It is apparent from the study that to be able to determine the carrier rate

one must have luck viz in finding the families that reproduce sufficiently It has shown also that it is still necessary to establish knowledge of new families If not we shall soon be left with a very small number of pedigrees

It is unlikely that the mode of inheritance of Leber s disease could be a special one applying to this disease only Better insight into the problems must be obtainable by comparison with pedigrees of other diseases transmitted through carriers The reason why ophthalmologists have devoted so much interest to the mode of inheritance of Leber s disease is that a knowledge of the predisposition is required for differential diagnostic purposes Collection of case histories by genetic studies has been needed to gain more knowledge of the pathognomy of the disease Therefore the large pedigrees embracing many generations have been established and have given rise to the discussion on the carrier rate If other diseases presented diagnostic difficulties which might necessitate the large pedigrees a few of them might perhaps also reveal a carrier rate so high that it could not be interpreted as being in accordance with the law of Mendel

The advantage of the present material is that the pedigrees have been recorded as completely as at all possible and that apart from recording the women s descendants it is known also which of the women are childless and whether the latter have passed the entire fertile age Those women who may have unknown descendants are marked by a special symbol and make up a minority The time of onset of the disease is for each individual patient stated in the pedigree as suggested by Julia Bell originally with a view to studies of anticipation and the influence of external factors upon the mechanism of manifestation but here used as information necessary for the calculation of the manifestation rate To keep this up the material must be reviewed about every 5 years If 15 years are allowed to elapse the review will require too much work and some material will inevitably be lost

The weak point of the material is that the majority of persons listed as healthy have not been examined ophthalmologically As the domiciles are so scattered that one examiner is unable to supervise them all it would be practical to institute collaboration between the eye departments in the entire country and examine members of the families in the nearest department gradually as they reach the age of 60 Notification of new cases to a central register would also be of great value Nation wide campaigns with the object of taking stock of the disease at 10 year intervals might inspire research

Strictly statistical calculations were not done on this material as it is difficult to set up rules according to which it should be analysed A satisfactory criterion of a non carrier has not been found The more exacting this criterion in respect to number of descendants and observation period the more undeterminable women will be found in the pedigree Incidentally the pedigrees would have to be analysed separately because in the case of one pedigree there is

one reason and in the case of another a different reason why they are not ideal

The worker who collects a material of persons with Leber s hereditary optic neuritis is bound to write about the mode of inheritance because genetic studies are used in collecting the material To bring research beyond this stage it is important thereafter to make the material accessible to the clinicians in their daily work so that the questions relating to the pathogenesis of the disease may arouse interest and be solved by a collaboration with pathologists biochemists physiologists and geneticists It would be reasonable to try first to elucidate the question whether the optic atrophy in Leber s disease is ascending or descending The high incidence of headache appears to indicate a cerebral disease It would be desirable to demonstrate the anatomical basis of the disease but it is difficult for the pathologists to get material for study The time of atrophy of the blood vessels in the disc does not give any decisive information about the seat of the primary lesion Biopsy from the visual pathways in the acute stage is contra indicated as it would harm the visual remnant Post mortem examination of the brain is usually not done because at the time of death the eye disease is so old that it seems irrelevant The similarity to the sequelae of alcohol poisoning suggests the association that the disease might be caused by a vulnerable enzyme system The amblyopia which may complicate the treatment of depression with monoamide oxidase inhibitors (*Emil Frandsen* 1962) is very like Leber s optic neuritis Studies on the pathogenesis of this visual damage might perhaps also throw some light upon the pathogenesis of Leber s optic neuritis Investigations of the monoamine oxidase activity in the retina and optic nerve have been performed by several authors during the period after 1956 most recently by Anja Mustakallio in 1967

The present material will afford help for the early diagnosis of the expected new cases of Leber s disease The diagnosis may then be done immediately after the onset of the disease even during the unilateral stage A few times doctors in these situations have felt that admission to hospital was unnecessary However there are many reasons for admission The patient is not up to being told the whole truth at once Among other things he may react violently when learning that others have been aware of the predisposition without telling him about it Remedies for migraine might be tested in the attempt to relieve the headache which may harrass some of the patients for the remainder of their lives The significance of physical exertion during the stage of neuritis to the visual end result has not been fully elucidated In cases where the disease starts on one side only it might be investigated in future whether the end result in the latter eye is better if the patient is spared physical exertion during the stage of neuritis This question must be settled before the early diagnosis perhaps results in the patients being made to work or is started on too early a training in an occupation for the blind

It is a fact that a number of the cases reported in the present study would not have been diagnosed as Leber s disease if this review of the pedigrees had not been carried out As a matter of course it is difficult to determine the centre of a central scotoma Indeed, a review of the case records shows that examination of the same patient at different times or by different examiners may result in different locations of the scotoma with centre in the visual axis centrocoecal quadrantic or hemianopic It must admitted that the clinician is faced with this difficulty and to consider the diagnosis of Leber s disease when ever coming across a scotoma involving the central part of the visual field Fixation ring on the perimeter as described by *Weve* (1942) and modified by *van Senus* (1963) is to be recommended If a patient with Leber s optic neuritis is subjected to exploratory craniotomy because the inherited predisposition is unknown and there is a suspicion of a juxtachiasmal lesion it is of course regrettable that the patient has to submit to an operation which has no therapeutic effect but it must be considered a reasonable step in the given situation It is maybe more unfortunate for the patient if his condition is diagnosed as alcohol amblyopia An alcoholic among patients with Leber s disease is in a very bad position His financial situation as well as his marriage may brak up and the visual loss is great The patient is lonely int al because his eye disease is interpreted as self inflicted The diagnosis of alcohol amblyopia will be entered on his papers in the public assistance office and disablement insurance court and will not be forgotten even though an inherited predisposition is demonstrated later

Still we have a possibility of getting nearer to the problems relating to Leber s disease by carefully noting all features of its acute stage and procuring accurate knowledge about its prevalence but presumably the desired results can be attained only by direct collaboration between geneticists and biochemists in elucidating the mode of inheritance as well as the mechanism of manifestation

Conclusion

In two out of 20 pedigrees both followed through 8 generations and representing 229 and 116 persons respectively it was not possible to demonstrate mothers who could be said with certainty to be free of the trait The results of studying these two pedigrees support the assumption that all women born in the pure female lineage are carriers This result cannot be disproved by the study of the other 18 pedigrees Thus the study has demonstrated that a carrier rate of 100 % does occur It has made probable but not definitely proven that this is a general rule

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DENDRITIC (HERPETIC) KERATITIS

II Follow Up Examination of Corneal Opacity (Opacity vascularisation Hudson Stahli s line sequelae of iritis)

BY

M S NORN

Cicatrisation is often seen in the cornea as a persistent sequela of dendritic keratitis Will such cicatrisation abate in the course of time? or is it more likely to exacerbate owing to further relapses? Has the chance of cicatrisation become reduced after introduction of 5 iodo 2 -deoxyuridine (IDU) treatment and which is the course in patients previously treated with steroids?

These are some of the questions that are of current interest because the disease is so relatively common and because several therapeutic possibilities exist including corneal transplantation

The study reported below comprised 109 patients followed up on an average 13 years after their first attack of dendritic keratitis

The composition of the material age and sex incidence recurrence rate and visual acuity at the follow up have been reviewed in a previous paper (*Norn* 1969)

It was pointed out that the series of patients was selected consisting solely of such as had been referred to an ophthalmologic unit for out patient treatment whereas not the great number treated by ophthalmic medical practitioners

The series must therefore be supposed to comprise the fairly grave cases of herpetic keratitis

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Corneal Opacity

The report includes 107 patients with previous attacks of dendritic keratitis two having been ruled out owing to corneal transplantation

All the follow up examinations were carried out by the author

The degree of opacity was estimated in the slit lamp also at subdued light in the room (slit lamp in darkroom) and by scleral scatter (intense slit lamp rays against *the sclera at the limbus observation of the cornea* through the slit lamp ocular and with the naked eye) thereby to disclose even the slightest opacity of the cornea

The area form and depth of the opacity have been entered in a diagram sketching the frontal and sagittal planes

Incidence and Site

Corneal opacity was detected in 91 cases (85 per cent) A sequela of keratitis is thus demonstrable in most cases even long after the attack

This result is in agreement with *Thygeson's* statement Scar formation is a principal if not invariable sequela of all corneal disease due to herpes simplex virus (1957)

The opacity was in most cases localized centrally covering the pupillary area When situated excentrically as was rarer it was most often found temporally (fig 1)

Morphology

In a great number of the eyes (*44 per cent*) an uncharacteristic, more or less

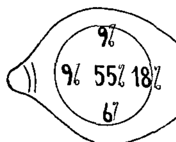


Fig 1

Localisation of the opacity in 91 patients who had had dendritic keratitis Percentage distribution In 4 per cent the opacity extended obliquely from one limbus to the opposite one.

disc shaped opacity was seen This was in some cases rather irregularly outlined, sometimes having off shoots which rarely were ramified

In 21 per cent there were found two or more disc formed opacities and in 10 per cent one or more punctate opacities

Only one fourth (25 per cent) of the patients showed opacities so characteristic that their appearance raised suspicion of previous dendritic keratitis Round opacities connected by off shoots were found and occasionally ramified opacities of the same shape as the typical dendritic keratitis pattern though somewhat broader

Transitional forms between the types described above were also seen

Area of Corneal opacity

The extension of the opacity in the frontal plane was sketched in a diagram and on the basis of this its size was roughly referred to one of the following categories, set up by *Mackenzie*

1) pinpoint size 2) less than 3 mm in diameter 3) less than one sixteenth of the corneal area 4) less than one eighth 5) less than one fourth 6) less than half 7) more than half of the total area of the cornea

The opacity covered on an average about 10 per cent of the corneal surface More than half of the cornea was covered in no more than 3 per cent and between one half and one fourth in 4 per cent (table I)

As might be expected there was no complete correlation between the area of the opacity and the *visual impairment* among other things because the site in relation to the centre is of decisive importance

Thus a patient with an opacity covering less than one fourth of the corneal area had a vision of only 6/36 while another had 6/6 with an opacity covering more than one fourth of the cornea

In table I the series has been divided into groups according to the *length of* the observation period The table shows that the opacity generally was the largest in the series with the longest observation period being on an average twice the size of that in the group observed for a short period

There were in other words no positive signs that an opacity may decrease in the course of time

The opacity increased in size with *rising number of attacks* The opaque area was on an average more than doubled in the group with over three attacks compared with that in the group with only one attack

One patient completely avoided development of an opacity despite ten attacks

The opaque area was seen to be independent of the patient s sex *and of the* age at first attack

The series has been divided into three groups on the basis of the therapy

instituted (steroid IDU or iodine cauterisation) Patients given more than one form of treatment have been counted in the corresponding groups The series would become too small if it were to include solely the patients given only one form of treatment

It is seen in the table that the area of the opacity generally was the largest in the patients treated with *steroids* This may be due to the fact that steroids were only given to patients whose disease had grown worse with impending or established metaherpetic development and who therefore were liable to more extensive opacity Steroids were administered in the hope of reducing corneal oedema and preventing further corneal opacity The final result was poorer than in the non steroid treated cases

The *IDU treated* and the *iodine cauteri ed* cases showed opacities approxi mately equal in size We must bear in mind however that the average obser vation period was considerably shorter for the IDU treated than for the others (Norn 1969) As moreover the recurrence rate seemed to be higher among the IDU treated these might be feared to get more extensive opacities in the course of time than the iodine cauterized

Depth of Corneal Opacity

The depth of the opacity has been roughly characterized as follows

I) thin II) less than one fourth of the total corneal depth III) less than half IV) less than three fourths and V) more than three fourths of the total corneal depth (tableI)

No correlation was noticed between the depth of the opacity and the *visual impairment* Of two patients both with an opacity so thick as to comprise more than three fourths of the cornea in depth one had 6/6 and the other 6/36

In the majority the opacity comprised only the most superficial portion of the corneal stroma In one case it was most intense in the deep layers while in eleven cases there was both superficial and deep condensation with a clearer zone in between and in three cases more irregular opaque bands in the stroma

In a small number of cases the cornea was definitely thinner at the site of the opacity with less anterior corneal curving

The opacity was relatively deep in patients observed for a long period and patients having had several relapses Further it was deeper after steroid treat ment than after IDU treatment and cauterisation in which latter groups it was n an average of the same depth

Vascularisation

The blood vessel invasion of the cornea has been graded as follows

A) minimal invasion B) invasion 1 3 mm from the limbus C) invasion of about half of the corneal area D) invasion comprising almost the entire corneal area

Blood vessel invasion was seen in half of all the eyes Blood vessel invasion without associated opacity was observed in one case only while 39 presented opacity without blood vessel invasion

The vascularisation tended to be most pronounced in the cases with the largest opacity (in area and depth) (table I)

A granular blood stream was in nearly all the cases seen to flow through the vessels invading the cornea Only few vessels showed no blood stream whatever (ghost vessels)

The vascularisation was on an average most pronounced in the patients observed for a long period and patients who had had many attacks compared with those who had had few or only one attack 28 out of 43 patients with only one attack were free from blood vessel invasion against no more than 6 out of 23 after three attacks

The possible influence of the *treatment* on blood vessel invasion is shown in table II No significant difference was found between the IDU treated the iodine cauterized and the total series

The observation period was as stated the shortest for the IDU treated Hence vascularisation must be feared to follow renewed relapses

One of the reasons for giving steroid was that of reducing the corneal oedema which constitutes a contributory factor in blood vessel invasion Nevertheless definitely increased vascularisation was found in the steroid treated group

Half of the total series had had a herpetic eruption on the *lips* at some time or other

No correlation was demonstrated between previous herpes of the lips on one hand *and vascularisation of the cornea and the area or depth of the* opacity on the other

Hudson Stahli s Line

Hudson Stahli s line is a thin brownish line which when typical runs a horizontal course under the centre of the cornea between the upper two thirds and the lower one third of the cornea

The line may be *found in normals in steadily increasing numbers* with maximum in the age class of 60 69 After the age of 70 the frequency falls again (*Norn* 1968 A) (table III)

Hudson Stahli s line was much more frequent in this series than among normals being present in 52 per cent of all who had had dendritic keratitis The

Table I

Size of opacity after dendritic keratitis dependence on observation period number of relapses therapy (steroid IDU or iodine cauterisation) Possible correlation of vascularisation with opacity 107 patients

The figures in the table indicate the *number of patient* except within the therapy survey where the figures represent percentage of treated in the group concerned

Grading of opacity area

1) pinpoint size 2) < 3 mm in diameter 3) < 1/16 of the corneal area 4) < 1/4 5) < 1/4 6) < 1/2 7) > 1/2 of the corneal area.

Grading of opacity depth

I) thin II) < 1/4 of the total corneal depth III) < 1/2 IV) < 3/4 V) > 3/4 of the total corneal depth

Grading of vascularisation

A) minimal B) extending 1 2 mm inwards from the limbus C) covering about half of the cornea, D) covering almost the whole cornea

	opacity area								mean	opacity depth					
	0	1	2	3	4	5	6	7	area	I	II	III	IV	V	Total
obs period															
5– 8 yrs	7	3	12	4	6	4	0	1	0 0,4	16	9	1	0	4	37
9–1 yrs	8	0	13	7	6	4	3	0	0 090	15	10	3	1	4	41
–13 yrs	1	1	4	5	8	7	1	2	0 174	8	5	2	3	10	29
number of attacks															
1	14	3	13	3	4	4	1	1	0 0C8	15	7	3	0	4	43
2 3	1	0	15	9	7	6	?	1	0 114	?0	11	1	?	6	41
–4	1	1	1	4	9	5	1	1	0 165	4	6	2	2	8	23
therapy (in per cent of treated in the group concerned)															
steroid	6	0	?	19	25	??	3	3	0 134	25	25	6	8	31	36
IDU	11	4	31	9	?6	13	2	4	0 108	33	31	6	4	15	54
iodine cauterisation	15		3	19	21	15	5	1	0 115	37	1	6	4	16	81
Total	13	4	7	15	19	14	4	3	0 10	36	2?	6	4	17	107
vascularisation															
none	15	4	19		8	1	0	0		25	11	3	0	0	54
A	0	0	6	1	1	1	0	0		5	2	1	0	1	9
B	1	0	4	6	11	5	1	2		9	9		1	8	30
C	0	0	0	1	0	5	?	0		0	2	0		4	8
D	0	0	0	1	0	3	1	1		0	0	0	1	5	6

Table II

Blood vessel invasion of the cornea dependence on therapy
The figures indicate in per cent the degree of vascularisation within the therapy group concerned
The degrees of vascularisation indicated by A D as in table I

vascularisation	0	A	B	C	D	Total
IDU	56	4	30	4	7	54
steroid	31	8	36	14	11	36
iodine cauterisation	47	10	28	10	5	81
Total	50	8	28	7	6	107

incidence being fairly independent of age the rising frequency with increasing years among normals was masked in this pathological series

The line was more frequently present in the pathological eye than in the contralateral (table III)

The distinctness of the line was roughly graded 1 to 5 (grade 1 being a very weak only just recognizable line grade 3 a moderately pronounced line and grade 5 a maximally pronounced line *An identical grading was employed by* the author in the normal series)

In the young age classes of the normal series the grade of Stahl's line when this was present at all averaged 1 0 and in the older age classes maximally 1 6

In the present pathological series with previous dendritic keratitis the line was on an average of grade 2 4 apparently independent of age Stahl's line was in other words much more pronounced than in the normal *series* and more than in the contralateral eye where the average was 1 4

Summarizing we may conclude that Stahl's line is much more frequent and more pronounced in patients who have previously had dendritic keratitis than in normals

Stahl's line hardly bears any direct relation to corneal opacity since cases were found showing opacity but not Stahl's line (39) and others showing Stahl's line but no opacity (4)

Stahl's line tends perhaps to occur more frequently and be more distinct in cases with a fairly extensive and deep opacity as well as vascularisation of the cornea

Of the patients with blood vessel invasion 59 per cent had Stahl's line against 41 per cent of those without vascularisation

Table III

Inci lence of Stahl s l ne among 106 patients wl o had had dendritic keratit s Incidence in the c ntralateral eye compared with that in a n n selecte l clinical series (700 patients)

age	per cent with Stahl s line			mean degr of Stahl s line		number of patients dendr
	seq of dendr keratitis	c ntralat	normal series	dendr	contral	
<10	50	18	0	2 3	1 0	2?
10-19	4?	?0	2	1 4	1 0	11
0-?9	6	0	11	2 9	0	13
30-39	?5	33	14	4 7	1 0	12
40-49	60	58	22	2 5	1 3	20
0-?9	47	50	31	2 4	2 0	17
60-69	73	63	44	? 0	1 6	11

Stahli's line was often seen to lie close to or within the region of a corneal opacity

Bizarre forms of Stahli s line were often seen two lines situated one above the other or beside each other a completely irregular serpentine line a Y shaped line a line having the form of a lying H and a horizontal line in the upper one third of the cornea Similar bizarre forms were however also met with in the normal series

Posterior Surface of Cornea

Folds of Descemet s membrane were found in four cases and a pigmented double line on the posterior corneal surface in one probably due to rupture of Descemet s membrane

In one case pigment flakes were seen on the posterior corneal surface

In seven cases residual precipitates were seen scattered on the posterior corneal surface Such were not observed in the contralateral normal eye

Aqueous flare was found in one case only in which the cornea was also stained by rose bengal suggesting active dendritic keratitis

Iris

In one case synechiae were seen between the iris and the lens and in one connective tissue membrane across the pupil as a sign of previous iritis

All the 107 patients were examined for iris transparency according to *Abrams*

In darkroom the patient fixes the light of the slit lamp (Haag Streit slit lamp No 900) The width of the slit is adjusted to just under the size of the pupil the axes of light and ocular are made to coincide and focusing is performed corresponding to the posterior surface of the iris The pupil will then reflect a red light as will also defects of the pigmentary layer of the iris Holes as small as 10 20μ corresponding to disappearance of a single cell are recognizable Different visual angles are employed to avoid disturbing corneal reflex (*Abrams Norn* 1968 C)

Examination using Abram s technique revealed defects of the pigmentary layer of the iris in 22 patients

Three were found to have fairly large local round or oval defects in the pig

mentary layer between the pupil and the periphery The defects were similar to such as may be found after iritis

One had a well defined sector formed defect and one a flat irregular defect likewise covering most of a sector

Four had defects in the pupillary border of the affected eye whereas not in that of the contralateral eye

Thus altogether nine patients displayed defects of the pigmentary layer of the iris which presumably were due to iritis caused by herpes virus

In two cases pigmentary defects were seen following antiglaucomatous operation (iridectomy iridencleisis)

Pupillary border defects alike in the two eyes were found in seven cases while in four cases fine punctate defects were fairly equally present inferiorly in the iris of both eyes These defects must be regarded as physiological

Signs of previous iritis were found in 22 of the 107 dendritic keratitis patients (characteristic iris defects synechiae precipitates etc) Active iritis was suspected in one case only

No case was referable to the steroid induced chronic kerato uveitis

Nearly half of the steroid treated patients of the present series belonged to the group with signs of previous iritis while only one fifth of the iodine cauterized and one sixth of the IDU treated displayed such signs

Corneal Transplantation

Two patients had had corneal transplantation performed one with a favourable result (vision 6/12 owing to immature cataract) In the other case the transplantation was complicated by recurrence of dendritic keratitis in the graft with consequent clouding (vision 6/36)

It has been found reasonable to consider corneal transplantation in 18 of the 10 cases in which the vision was under 6/18

However in three cases operation was not advised One patient had the first attack of keratitis as early as the age of 4 5 and the eye is possibly amblyopic one was found unfit for psychic reasons and one for social (alcoholic)

Four had previously been interested in corneal transplantation but they had now become so used to the impaired vision of one eye that they no longer desired operation

Ten patients were not interested in corneal transplantation because they managed well visually with the healthy eye

One desired operation (1/24 of both eyes)

Thus only three out of 109 patients with previously diagnosed dendritic keratitis had been subjected to or desired corneal transplantation

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Three were found to have fairly large local round or oval defects in the pig

The size of the opacity and the degree of vascularisation might therefore be conceived to be the least alarming for the patients treated by iodine cauterisation alone

Hudson Stahly s line is more frequent and more pronounced among patients who have had dendritic keratitis than among normals The difference is particularly significant in the young age groups where the line is rarely seen in normals.

I concluded on the basis of a pathological series comprising 364 patients that the line is relatively frequent in association with uveitis in particular anterior uveitis and that the line may bear relation to a corneal cicatrix in extremely few cases only (*Vorn* 1968 B)

The frequent occurrence of Hudson Stahli s line after dendritic keratitis is perhaps in part explainable by the high incidences of corneal opacity and iritis in this series On the other hand other factors bearing relation to the herpes virus may also have played a role The cause of Stahli s line is still obscure

Only 2 per cent of the total series have been subjected to corneal transplantation and only few of the others are likely to have this operation performed This low number in spite of many grave cases is due to a hesitating attitude towards transplantation among patients whose contralateral eye is intact.

In a future paper the results will be reported of examinations concentrating on the precorneal film vital staining and Fischer Schweitzer s polygonal fluorescein pattern carried out on the present series The object of these examinations have been to clarify if possible, whether such investigations into the superficial pathology of the cornea can yield further details of clinical value in the control of patients having had dendritic keratitis

Summary

A series of 109 patients who had had dendritic keratitis (the first attack on an average 13 years previously) have been followed up

Corneal opacity was seen in 85 per cent most often localized centrally It was ramified in no more than one fourth of the cases and covered on an average 10 per cent of the corneal area

Blood vessel invasion was found in half of the affected eyes

The size of the opacity (area and depth) and the vascularisation were seen to become aggravated with increasing length of the observation period as well as after some relapses after treatment with steroids and probably also after IDU treatment

The result of the present investigation suggested that iodine cauterisation gives the least opacity

Local Tanderil Treatment

In an attempt to reduce the corneal opacity I treated 18 of the most gravely *affected eyes with oxiphenbutazonum NFN (tanderil Geigy ointment 10%* an anti inflammatory agent hydroxyphenylbutazone)

In one case recurrence of dendritic keratis was noticed before the treatment and in five punctate staining (fluorescein or rose bengal) prior to the treatment The remainder showed no signs whatever of activity on prescription of the ointment

This therapy was not followed by activation of the dendritic keratitis On the other hand no improvement was seen either presumably because the treatment was instituted too late

Application of tanderil at the active stage has not been tried

Such investigations are under preparation (Geigy s workshop on opthalmology in Kandersteg jan 1970)

Discussion

The series under review was in some measure selected constituting fairly grave cases of dendritic keratitis This may possibly account for the fact that sequelae of previous iritis were seen in so many patients (21 per cent)

The prognosis of dendritic keratitis is poor In particular the condition has been found to deteriorate with increasing length of the observation period oving to frequent relapses while conversely signs of spontaneous clearing up of the cornea have never been observed The longer the observation period the more does the opacity grow in area and depth with associated increasing vascularisation

The visual impairment has been shown previously to be the greatest after steroid treatment (*Norn* 1969) In the present series this group was found to be burdened with a larger opacity area and depth a more intense vascularisation and more frequent signs of iritis than the other groups

As pointed out above these phenomena might all theoretically be accountable for by the fact that steroid is preferably administered to the severest cases in which the prognosis already is particularly poor However *Thygeson* (1967) has shown that steroid is contraindicated in cases of dendritic keratitis

As for IDU treatment the degree of visual impairment the size of the opacity and the degree of vascularisation seemed to be independent of the treatment However the average observation period was shorter for this group than for the remaining series It is therefore to be feared that further relapses may render the final result poorer than that for the patients not given IDU

The size of the opacity and the degree of vascularisation might therefore be conceived to be the least alarming for the patients treated by iodine cauterisation alone

Hudson Stahly s line is more frequent and more pronounced among patients who have had dendritic keratitis than among normals The difference is particularly significant in the young age groups where the line is rarely seen in normals.

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Blood vessel invasion was found in half of the affected eyes

The size of the opacity (area and depth) and the vascularisation were seen to become aggravated with increasing length of the observation period as well as after some relapses after treatment with steroids and probably also after IDU treatment

The result of the present investigation suggested that iodine cauterisation gives the least opacity

Hudson Stahli s line was found in 52 per cent apparently equally often in the different age groups and more frequently than in a normal series where the line is a fairly rare phenomenon especially in the young age classes

Signs of previous iritis were seen in 21 per cent (defects of the pigmentary layer of the iris synechiae precipitates etc)

Acknowledgment

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DENDRITIC (HERPETIC) KERATITIS

III. Follow up Examination of the Percorneal Film, Fischer-Schweitzer's Fluorescein Pattern and Vital Staining

BY

M. S. NORN

Dendritic keratitis is an often painful disease which frequently recurs.

The author of the present paper summoned 107 patients who had previously had herpetic keratitis to a follow up, partly to see whether any of these patients presented recurrence, recognized or symptom free, at the follow up, and partly to make out how often sequelae of keratitis are detectable in the forms of corneal cicatrices, blood vessel invasion, impaired vision, etc.

The selection and composition of the series as well as the recurrence rate, observation periods, opacity, vascularisation, Hudson-Stahli's line and visual impairment have been described in previous papers (*Norn* 1969 C and D).

In the present paper an account is given of the result of vital staining at the follow up. Two vital stains were used (fluorescein and rose bengal). At the same time I took the opportunity of examining the vital stained precorneal film. Further, I massaged the eyelid for the purpose of eliciting the fluorescein stained corneal mosaic pattern which is seen in normals but is absent in the presence of pathological processes in the superficial part of the cornea.

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Wetting time

The precorneal film is the thin fluid layer covering the cornea (*N Ehlers*)

The precorneal film is the thickest immediately after blinking It then grows increasingly thinner finally to burst A hole is formed which is most plainly visible in the fluorescein stained precorneal film when this is observed in the slit lamp with cobalt-filtered light

The wetting time means the interval from the conclusion of blinking to the start of hole formation in the precorneal film

On examining a *normal series* with fluorescein stained precorneal film I found a mean wetting time of 30 seconds

The wetting time was independent of addition of 0 3 % oxibuprocain chlor NFN (novesin Wander) (*Norn* 1969 A)

For the present follow up of patients with previously diagnosed dendritic keratitis the same technique was employed as for the above mentioned examination of a normal series

The patient is placed in front of the slit lamp 0 125 % fluorescein with 0 3 % novesin added is instilled The patient blinks twice or more The precorneal film is observed in the cobalt filtered light of the slit lamp and the time elapsing until hole formation is first visible is measured using a stop watch

The patient is requested to keep the eye open voluntarily during the examination The lids are not supported by the examiner

A total of 107 patients who had had dendritic keratitis were examined The mean wetting time was 17 seconds or considerably shorter than that in a normal series where using the same technique I found it to be 30 seconds

Even though most of the patients no longer had active keratitis (*see later*) many were found to have a pathological reduced wetting time

In the present series there was no sex difference (45 women had a wetting time averaging 18 seconds and 62 men 16 seconds)

In this respect the series thus differs from the normal series where the wetting time was considerably shorter for women than for men (24 against 36 seconds)

The normal longer wetting time for men becomes reduced or even eliminated *in a pathological series* where both sexes have a reduced wetting time

The shorter wetting time in patients who have had dendritic keratitis might be due to the frequent occurrence of an opacity which must be supposed to constitute a poor *foundation of the precorneal film*

Table I shows however that the wetting time also was reduced in the cases where no opacity was detectable (averaging 20 seconds)

The wetting time is perhaps the shortest in the cases with the deepest *opacity* whereas the area seems to have no influence

In cases with corneal opacity from other causes no pathological wetting time was demonstrable (*Norn* 1969 A)

Permanent Holes in the Precorneal Film

Permanent holes in the precorneal film are such as are recognized immediately on concluded blinking These holes are seen at the same site on re examination unlike the holes occurring after a certain interval

Permanent holes (wetting time zero) are only found in pathological cases (*Norn* 1969 B)

In the present series permanent holes were found in 15 per cent of the 107 examined and only in cases with corneal opacity

In five cases the dry spot in the precorneal film was noticed at the site of a small fluorescein stained erosion or keratitis while in two it was due to a visible small epithelial vesicle and in one to corneal oedema

Two patients presented a rose bengal stained area at the site of the dry spot and one a calcareous spot in the opacity

Thus in eight cases a reasonable pathological explanation could be given of the permanent hole formation in the precorneal film a corneal defect (erosion keratitis) or a vesicle on the cornea. In another three cases there was a possible explanation.

In the remaining five cases the dry spot was likewise seen over an opacity

Table 1

Possible dependence of the *wetting time* on the depth and area of the opacity 107 patients who had had dendritic keratitis

Opacity depth	Wetting time	No of pts	Opacity area	Wetting time	No of pts
no opacity	0	16	no opacity	20	16
thin	0	39	< 3 mm	21	33
< 1 4	1	4	< 1/16	11	16
<	8	6	< 1 8	15	0
< 3 4	11	4	< 1/4	10	15
> 3 4	14	18	> 1/4	23	7
Total	17	10		1	10

in four cases at the site of a peripheral sparing in Fischer Schweitzer s pattern and in one at a corresponding central sparing (see later)

In these cases the dry spot in the precorneal film must also be supposed to be accountable for by a pathological process which however is not detectable otherwise than by a permanent hole formation in the precorneal film remaining at the same site on repeated examination

The permanent hole formation can thus give additional information on the pathology of the cornea of patients with previous attacks of dendritic keratitis On the other hand this pathological condition is only disclosed in the cases with presence of corneal opacity No instance has been found of a permanently dry hole in an otherwise normal cornea

The permanent hole formation and wetting time seem to be independent of the *therapy* given though with a tendency to most pronounced pathological values among the steroid treated

The mean wetting time in the steroid treated series was 14 seconds in the IDU treated 19 seconds and in the iodine cauterized 16 seconds while in the total series it was 17 seconds

Fischer-Schweitzer s Polygonal Pattern

Fischer demonstrated in 1928 that by rubbing the cornea through the closed lid a net like pattern could be provoked in strong light reflected from the cornea on a screen

Schweitzer showed that the same net like pattern can be produced without use of any special apparatus by rubbing the cornea after instillation of 0 2 % fluorescein into the conjunctival sac The pattern can be studied in cobalt filtered light in the slit lamp

The pattern is always present in normals but absent over a corneal opacity or nubecula and occasionally also in cases of corneal oedema and erosion

The pattern has been described later in relation to clinical series by *Bron* and by *Norn* (1968) in the latter paper named Schweitzer s pattern

Schweitzer has remarked to this (personal communication) that I would strongly suggest that this pattern should be called after Fischer who taught me ophthalmology when I was a student If any work was fundamental it was his

The term Fischer Schweitzer s pattern has therefore been preferred in this paper

Examination for Fischer Schweitzer s fluorescein pattern was carried out as follows

0 125 % fluorescein with 0 3 % novesin added was instilled into the conjunctival sac The patient was placed in front of the slit lamp The cornea was

massaged gently and rapidly with the examiner s finger on the closed lid The cornea was examined immediately after in cobalt filtered light in a Haag *Streit slit lamp* No 900

If a mosaic pattern was not seen or was indistinct the massage and the examination were repeated if necessary after renewed staining with fluorescein or with a mixture of 1 % fluorescein and 1 % rose bengal

Result

Fischer Schweitzer s pattern was pathological in most of the examined patients (79 per cent) who had had dendritic keratitis

The pattern was totally absent in eight of the 107 examined even after repeated examination while it was normal in the contralateral eye (table II)

In the remaining cases more or less of the fluorescein pattern was absent There were found one or more rather central areas with no pattern surrounded by normal pattern (fig 1) or a peripheral sparing (fig 2) or the fluorescein pattern was so greatly reduced that only one or more islets were seen on an otherwise pattern free cornea

The sparing of the pattern often corresponded to a corneal opacity In some instances it covered exactly the same area as the opacity (fig 1) while in others it was a little smaller or larger than the opacity

However cases may be found with a normal Fischer Schweitzer s pattern despite presence of a distinct opacity This was so in 12 patients (six punctate or small thin opacities five fairly large central opacities extending through at

Table II
Pathological *Fischer Schweitzer s* fluorescein pattern in 107 *patients with previous* dendritic keratitis

	number of patients
totally absent	8
residual islet(s)	31
one central sparing	22
two or more central sparings	10
peripheral sparing	10
central and peripheral sparing	3
Total number with pathological Fischer Schweitzer s fluorescein pattern	84

in four cases at the site of a peripheral sparing in Fischer Schweitzer s patter
and in one at a corresponding central sparing (see later)

In these cases the dry spot in the precorneal film must also be supposed t
be accountable for by a pathological process which, however, is not detectabl
otherwise than by a permanent hole formation in the precorneal film remainin
at the same site on repeated examination

*The permanent hole formation can thus give additional information on th
pathology of the cornea of patients with previous attacks of dendritic keratiti*
On the other hand this pathological condition is only disclosed in the case
with presence of corneal opacity No instance has been found of a permanentl
dry hole in an otherwise normal cornea

The permanent hole formation and wetting-time seem to be independent o
the *therapy* given though with a tendency to most pronounced pathological va
lues among the steroid treated

The mean wetting time in the steroid treated series was 14 seconds in th
IDU treated 19 seconds and in the iodine cauterized 16 seconds while in th
total series it was 17 seconds

Fischer-Schweitzer s Polygonal Pattern

Fischer demonstrated in 1928 that by rubbing the cornea through the closed lid
a net like pattern could be provoked in strong light reflected from the cor
nea on a screen

Schweitzer showed that the same net like pattern can be produced without
use of any special apparatus by rubbing the cornea after instillation of 0 2%
fluorescein into the conjunctival sac The pattern can be studied in cobalt fil
tered light in the slit lamp

The pattern is always present in normals but absent over a corneal opacity
or nubecula and occasionally also in cases of corneal oedema and erosion

The pattern has been described later in relation to clinical series by *Bron*
and by *Norn* (1968) in the latter paper named Schweitzer s pattern

Schweitzer has remarked to this (personal communication) that I would
strongly suggest that this pattern should be called after Fischer who taught me
ophthalmology when I was a student If any work was fundamental it was his

The term Fischer Schweitzer s pattern has therefore been preferred in this
paper

Examination for Fischer Schweitzer s fluorescein pattern was carried out as
follows

0 125% fluorescein with 0 3% novesin added was instilled into the con
junctival sac The patient was placed in front of the slit lamp The cornea was

In two of these cases Fischer-Schweitzer's pattern was totally absent (normal pattern contralaterally).

Two showed sparing of the pattern inferiorly at the site of a previous dendritic keratitis as seen in the case record.

In one case two islets were seen nasally in the pattern at the site of previous keratitis (fig. 3).

Fischer-Schweitzer's technique thus serves to evidence – even in some cases without opacity – not only that a patient has had keratitis but also where this was located.

The method is therefore suitable as a supplementary test in cases where it is desired to know whether a patient may have had dendritic keratitis, e.g. before instituting local steroid treatment or when examining a potential contact lens wearer.

However, *of the 107 patients included in this study eleven (10 per cent) displayed* neither opacity nor an abnormal Fischer-Schweitzer's pattern.

An only doubtful correlation was noticed between the *treatment* given and a pathological Fischer-Schweitzer's pattern (92 per cent of the steroid treated, 83 per cent of the IDU treated and 79 per cent of the iodine cauterized had a pathological pattern).

Vital Staining

Vital staining was performed by instillation of 0.01 ml of a mixture containing 1 % fluorescein and 1 % rose bengal (*Norn* 1964).

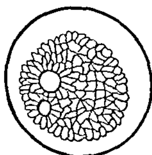


Fig. 3.

A man had a typical dendritic keratitis nasally of the *left eye* at the *age of 34*. At a follow up 11 years later the cornea seemed to be normal (no opacity nor nubecula, not at scleral scatter either, no vascularisation nor *Hudson-Stähli's* line, corneal sensitivity normal).

Fischer-Schweitzer's fluorescein pattern showed two distinct defects at the site of the previous keratitis.

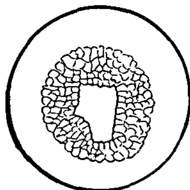


Fig 1

A woman had dendritic keratitis at the age of 28 No recurrence A follow up 7 years later revealed superficial opacity and central sparing of a pronounced *Fischer Schweitzer s* fluorescein pattern corresponding exactly in area and shape to the opacity

most one half of the corneal depth and one peripheral opacity extending through more than three fourths of the corneal depth)

The present material allows of no conclusions regarding a correlation between a certain site and depth of the opacity on one hand and occurrence of a defect of Fischer Schweitzer s pattern on the other

Five patients (5 per cent of the total series) were even found to have a pathological Fischer Schweitzer s pattern but no visible opacity

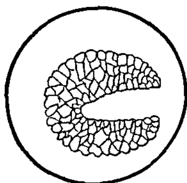


Fig 2

A woman had dendritic keratitis at the age of 43 No recurrence A follow up 7 years later revealed a large transverse superficial opacity with a ramified offshoot towards 1 o clock

Fischer Schweitzer s fluorescein pattern showed peripheral sparing over an area corresponding approximately to that of the opacity whereas the pattern was normal across the offshoot from the opacity

In two of these cases Fischer Schweitzer's pattern was *totally absent* (*normal pattern contralaterally*).

Two showed sparing of the pattern inferiorly at the site of a previous dendritic keratitis as seen in the case record.

In one case two islets were seen nasally in the pattern *at the site of previous* keratitis (*fig 3*).

Fischer Schweitzer's technique thus serves to evidence – even in some cases without opacity – not only that a patient has had keratitis but also where this was located.

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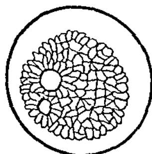


Fig 3

A man had a typical dendritic keratitis nasally of the left eye at the age of 34. At a follow up 11 years later the cornea seemed to be normal (no opacity nor nubecula, not scleral scatter either, no vascularisation nor Hudson Stahli's line, corneal sensitivity normal).

Fischer Schweitzer's fluorescein pattern showed two distinct defects at the site of the previous keratitis.

The cornea was studied partly in cobalt filtered light (interrupted continuity of the cornea fluoresces because fluorescein penetrates through the rupture) and partly in white light (degenerate cells are stained red by rose bengal)

Vital staining was observed in 35 per cent of the 107 patients who had previously had dendritic keratitis and had now been summoned for a follow up

In two cases a fresh recurrence of dendritic keratitis showing a ramified pattern was found which was stained both by fluorescein and by rose bengal.

In five cases local pathological staining was seen at the site of a previous attack of dendritic keratitis in two cases on account of vesicles in two due to erosion and in one to corneal oedema All the pathological processes were stained by fluorescein and by rose bengal

Eight patients presented pronounced extensive punctate fluorescein and rose bengal staining of unknown cause

In three cases fluorescein staining was observed which might be due to the examination itself linear or slightly crescent erosion

19 patients showed punctate rose bengal staining in three cases in a pronounced degree and spread over the whole cornea while in the remaining it was most often localized in a limited space inferiorly and inferonasally as may be seen even in normals

By means of vital staining we disclosed recurrence of dendritic keratitis in two cases pathological processes constituting sequelae of dendritic keratitis in five and abnormal corneae in eleven others out of 107 patients

No correlation was demonstrated between the area of the opacity and the frequency of vital staining

Among the steroid treated vital staining was recorded in 44 per cent against 33 per cent among the IDU treated and the iodine cauterized This difference may be due to steroid having preferably been prescribed in the grave cases

Permanently dry holes were most frequently found on corneae that were vital stained This is due to the fact that erosions and vesicles constitute the basis of such holes in the precorneal film Dry spots were found in 32 per cent of the vital stained corneae whereas in no more than 15 per cent of the total material

Discussion

The present investigation gave the result that the cornea very rarely escapes permanent sequelae of dendritic keratitis

Corneal opacity or nubecula has been found to occur in 85 per cent (Norn 1969 D)

A pathological Fischer Schweitzer s pattern in the form of a defective or totally absent mosaic has been observed in 79 per cent In 5 per cent this pa

thological pattern was not accompanied by opacity In other words 90 per cent of all the corneae examined displayed opacity and/or a pathological Fischer Schweitzer s pattern.

The mean wetting time was reduced in these patients likewise indicating that the corneae rarely becomes normal after a dendritic attack

Permanently dry holes in the precorneal film were found in 15 per cent In these cases opacity was also seen however Accordingly this method did not disclose an additional number of pathological cases in the present series Still further information was obtained on the pathology of the cornea

In another series I found examples to the effect that residual erosion is only detectable by this method (*Norn* 1969 B)

At the follow up vital staining revealed active recurrence of dendritic keratitis in 2 per cent *These patients had had a sensation of irritation of the eye* for 24 hours and three weeks respectively No cases were observed of asymptomatic dendritic keratitis

Pathological vital staining was noticed in several cases (17 per cent) as a sign of a continued pathological state after dendritic keratitis

These findings showed that even during an apparently recurrence free period with no symptoms the cornea may in many instances be of a poor quality with residual corneal oedema and interrupted continuity of the epithelium a condition which presumably adds to the chance of renewed recurrence

The present follow up was carried out on a selected series of patients in as far as it only comprised patients referred to a hospital out patient department

A less severely affected series might possibly contain fewer cases showing pathological changes

In such a series a follow up examination must however also be expected to reveal several pathological cases when the greatest number available of clinical methods are employed

To judge from the results of the present study the prognosis of dendritic keratitis is strikingly poor

The results of corneal sensitivity measurements on the same series will be reported in a final paper

Summary

A follow up examination of 10[illegible] patients who had previously been affected with dendritic (herpetic) keratitis showed the precorneal film to have a reduced *wetting time* (average 1[illegible] seconds against 30 seconds in a normal series measured from concluded blinking to occurrence of a hole in the fluorescein stained precorneal film)

A *permanent hole* in the precorneal film was found in 15 per cent due to erosion epithelial vesicle keratitis In some cases it was of unknown cause

Fischer-Schweitzer s fluorescein pattern was pathological in 49 per cent (totally absent in 7 per cent) In 5 per cent no opacity was seen at the same time The abnormal pattern was thus the only indication of a pathological process in the cornea concerned and of the site of this

Vital staining (fluorescein or rose bengal) was observed in 35 per cent At the time of the follow up 2 per cent had active keratitis about 15 per cent sequelae of keratitis in 5 per cent in the forms of vesicle erosion or oedema

No more than 10 per cent presented no sequelae of the previous dendritic keratitis

Acknowledgment

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Department of Ophthalmology, Kommunehospitalet, Copenhagen
(Heads: P. Brændstrup and M. S. Norn)

LOCALISATION OF BACTERIA ON SINGLE EYELASHES

BY

M. S. NORN

During an operation one may happen to touch an eyelash with an instrument or suturing material. Further, one may not infrequently find an eyelash within the field of operation. How great is the risk of infection during the operation in such cases?

As is well known, staphylococci are often present along the palpebral border (*Burford, Allansmith et al.*). The contamination of the individual eyelash and the sites of the bacteria on this do not seem to have been examined previously, however.

In the course of time attempts have been made in different ways to avoid contamination from the eyelashes during operation.

Pre-operative cutting of the lashes is employed in many places. *Allen*, in a leading article on the practical aspects of ocular infection, called attention to the fact that such cutting hardly is of any value in practice. It is perhaps a ritual rather than a rationale.

Newton et al. advise against cutting because they find that suturing material is more easily caught by the stubble left, and because the base of the hair may be infected. Newton recommends sewing of moist gauze bits on to the upper and lower lids to cover all the lashes during the operation.

Elastic covering is perhaps more practical, e.g. with *steridrapes*.

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Some specula are constructed so as to cover the eyelashes as far as possible. Many surgeons apply prophylactic antibiotic ointment the night before the operation

Gowen (1934) showed that bacteria on the eyelid constitute a grave source of infection of the conjunctiva the bacteria being transferred *via* the eyelashes

This route of infection was demonstrated by spreading a culture of *Bacterium progidiosus* on the skin of the lower lid The bacteria were recovered on the lashes of the lower lid and in the conjunctiva Bacteria spread on the upper lid on the other hand were not transferred to the lashes or the conjunctiva. The transfer is supposed to proceed during blinking when the lower row of lashes becomes bent so as to touch the skin

Barfoed (1953) studied the bacterial flora in the conjunctiva and along the palpebral border in 521 cases Bacteria for culture from the eyelid were obtained by intensive rubbing with a sterile broth moistened cotton swab

Staphylococcus albus were detected on 84 6 per cent of the eyelids and *Staphylococcus aureus* on 23 6 per cent In the conjunctiva on the other hand the former species were found in no more than 37 5 per cent and the latter in 7 6 per cent Accordance between the findings on the skin of the eyelid and in the conjunctiva was found in 27 per cent only

The differences between the bacterial flora of the skin and that of the conjunctiva must be supposed to be due to environmental factors Staphylococci can break down fatty acids being therefore able to live in a sebaceous environment Staphylococci have their headquarters in pilosebaceous units (*Marples*)

Inside the eyelid only small amounts of fat are present in the forms of a thin possibly monomolecular fatty layer in the precorneal film (*N Ehlers*) and drops of fat on the mucous thread in the inferior conjunctival fornix (*Norn* 1969 A)

Evidently the mucous layer of the conjunctiva is no optimum environment for staphylococci Corynebacteria on the other hand do well and in normals these will often oust bacteria coming from the skin

Staphylococci on the palpebral skin may be the cause of blepharitis which nearly always is complicated by conjunctivitis and possibly also of staphylococcus induced punctate or more rarely marginal keratitis (*Thygeson* 1941 1946) However attempts to combat staphylo blepharitis with mercurial ointment (Penotrase) were unsuccessful in as far as the ointment could not cure the associated staphylococcal infection of the conjunctiva (*More* 1968)

Hairs are rather often found in the inferior fornix Thus microscopic examination revealed hairs (eyelashes hairs from eyebrow and elsewhere) in 12 per cent of 198 eyes (Polarisation microscopy – *Norn* 1969 B)

The object of the present study was to clarify how often the individual eyelash is contaminated and where the bacteria are situated and to map out the resistance pattern of the bacteria

Method

The individual eyelashes were epilated with sterile epilation tweezers singed between each two epilations The lash was transferred to an agar slide where the root alone was rubbed against the slide over a distance of 3 4 cm The lash was thereafter laid on the slide in its entire length

The medium used was Uricult N agar containing beef peptone liver proteo lysate salts and agar (Uricult Orion Helsinki Finland)

The slide was incubated at 35° for 48 hours

The slide was examined after 48 hours The number of bacterial colonies was recorded and the growth of bacteria from the eyelashes and their sites were outlined The individual colonies were isolated and identified and their re sistance was determined

Material

Examination of four eyelashes from each eye was aimed at one medial and one lateral from the upper lid and one medial and one lateral from the lower

The investigation comprised 33 eyes from 17 patients None of these patients showed any signs of infectious conjunctivitis The clinical diagnoses were re tinal detachment in four cases cataract in four glaucoma in two uveitis in one chronic simple conjunctivitis in one while five were normal subjects

Five had not been treated with antibiotics or chemotherapeutics

Results

In some cases more than one lash was epilated at a time In 17 cases the two lashes were lying so close together that they presented a common bacterial growth having therefore been reckoned as one in the report

In 21 cases an extra isolated eyelash appeared on the slide This was in cluded in the investigation which accordingly comprised 153 lashes

Culture revealed *Staph albus* and a few strains of *Staph aureus* as well as *Bacterium anitratum*

The first cultivation on Uricult gave cocci round 119 lashes (77 per cent of the total number)

On further cultivation and resistance determination bacterial growth was seen again in 96 cases (63 per cent)

Staph albus were isolated from 56 per cent of all the lashes *Staph albus*

Some specula are constructed so as to cover the eyelashes as far as possible Many surgeons apply prophylactic antibiotic ointment the night before the operation

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The differences between the bacterial flora of the skin and that of the conjunctiva must be supposed to be due to environmental factors Staphylococci can break down fatty acids being therefore able to live in a sebaceous environment Staphylococci have their headquarters in pilosebaceous units (*Marples*) Inside the eyelid only small amounts of fat are present in the forms of a thin possibly monomolecular fatty layer in the precorneal film (*N Ehlers*) and drops of fat on the mucous thread in the inferior conjunctival fornix (*Norn* 1969 A)

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The object of the present study was to clarify how often the individual eyelash is contaminated and where the bacteria are situated and to map out the resistance pattern of the bacteria

the root of the lash in agreement with the observation that the hair follicle constitues the headquarters of *Staph albus* Note that the tip of the lash more rarely is infected

The tip of the lash was infected in 18 cases To these may be added 38 lashes contaminated in their entire length Thus a total of 56 lashes had bacteria at the tip

If the lashes had been cut close to the root as is often done pre operatively there would have been a risk of contamination from the stubble in 52 cases where the root was infected plus 38 cases with the whole lash infected This gives a total contamination risk from 90 eyelashes

There is in other words a *theoretically increased risk of contamination after cutting of the lashes*

For 27 out of 153 eyelashes bacterial colonies were seen in the *track* on the agar slide after rubbing of the root across the slide The numbers of colonies were 1 2 in eleven 3 5 in four 6 8 in four 9 10 in four about 50 in two 70 in one and about 1000 in one

Chemoresistance

As shown in table II practically all the *Staph albus* strains were susceptible to erythromycin but often relatively or completely resistant to penicillin and sul phonamide

44 per cent of the strains were resistant to tetracycline and 43 per cent to chloromycetin while 23 per cent were resistant to streptomycin

The patients not treated previously with antibiotics or chemotherapeutics showed approximately the same resistance pattern (table II)

The few *Staph aureus* strains found were susceptible to all the antibiotics tried except two strains which were resistant to penicillin

We may conclude that rational treatment against bacteria on the eyelashes can be carried out with erythromycin while chloromycetin and tetracycline are less suitable and penicillin and sulphonamide unsuitable

Discussion

The finding of many chloromycetin resistant *Staph albus* strains was sur prising

In 1963 *Gregersen* studied the resistance pattern of bacteria isolated from

were found on one or more lashes from all the patients except one who in return harboured *Staph aureus*

In four eyes *Staph albus* were not detected while 15 eyes showed one *Staph albus* strain and seven two different strains to judge from the chemoresistance pattern Four eyes harboured three strains Finally, four five and six strains *with different* patterns were detected in one eye each

In 14 eyes there were found not less than two *Staph albus* strains with different chemoresistance patterns judged by examination of four eyelashes or more from each eye On an average 2 9 strains were found per eye The numbers of strains averaged 1 7 on the upper lid and 1 9 on the lower Further the medial pair of lashes contained on an average 1 9 strains and the lateral 1 7 strains

The figures suggest that the various eyelashes of an individual may harbour two or more staphylococcal strains accumulated within different parts of the row of lashes

Staphylococcus aureus were found in 5 per cent of all the lashes namely in four eyes of three patients Two patients harboured only one phage type each (type 52/80 u and 42 E/47/53/54/75/77/83 A/84/85/6077/92)

In the third patient there were found two phage types in one eye (52/52 A/80 and 84/6551/592) and a different phage type in the other eye (3 Cu)

Thus five phage types were seen

In one eye there were found two *Staph aureus* strains differing in susceptibility while in the remaining eyes only one pattern was seen

Bact anitratum were isolated from 1 per cent of all the eyelashes i e in two eyes of two patients with only one resistance pattern per eye

The site of the bacterium on the epilated eyelash is shown in table I

It is seen in the table that the bacteria most often are localized in or round

Table I

Sites of the bacteria on the epilated eyelash

	Staph albus	*Staph aureus*	Total
primary growth from the root	47	5	52
middle of the shaft	10	1	11
the tip	18	0	18
the whole length	36	2	38
Total	111	8	119

the root of the lash in agreement with the observation that the hair follicle constitutes the headquarters of *Staph albus* Note that the tip of the lash more rarely is infected

The tip of the lash was infected in 18 cases To these may be added 38 lashes contaminated in their entire length Thus a total of 56 lashes had bacteria at the tip

If the lashes had been cut close to the root as is often done pre operatively there would have been a risk of contamination from the stubble in 52 cases where the root was infected plus 38 cases with the whole lash infected This gives a total contamination risk from 90 eyelashes

There is in other words a *theoretically increased risk of contamination after cutting of the lashes*

For 97 out of 153 eyelashes bacterial colonies were seen in the *track* on the agar slide after rubbing of the root across the slide The numbers of colonies were 1 2 *in eleven 3 5 in four 6 8 in four 9 10 in four about 50 in two* 70 in one and about 1000 in one

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Discussion

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Table II

Resistance pattern of bacterial strains cultured from eyelashes

	number of strains	*penicil*	*sulpha*	*strepto*	*tetra*	*chloromyc*	*erythr*
Staph aureus	9	2	0	0	0	0	0
Staph albus	128	105	98	30	56	55	2
Staph albus in per cent	128	82	77	23	44	43	2
Staph albus from non anti biotic treated pts in per cent	42	81	83	19	40	38	0

the nasal muccosa of employees doctors and nurses attached to the Department of Ophthalmology Kommunehospitalet He found 26 *Staph aureus* strains all susceptible to chloromycetin and 26 *Staph albus* strains of which only three were resistant to chloromycetin

S E Lorent en in a similar investigation from 1967 achieved practically the same results as *Gregersen* (only one chloromycetin resistant *Staph aureus* strain out of 17)

Lorentzen concluded that though chloromycetin has been used as the antibiotic of choice in this Department since 1957 chloromycetin resistant *Staph aureus* strains have not developed in the nasal flora of the staff living in a chloromycetin containing environment

The observation of 43 per cent resistant *Staph albus* strains cultured from eyelashes raises suspicion of development in the unit of chloromycetin resistant strains This development is possibly related to increasing use of chloromycetin also as a drug for general oral treatment It will therefore be a matter of interest to undertake another examination in a few years of the nasal flora in this unit

The investigation showed that *Staph albus* is a very frequent finding on the individual eyelash It is therefore surprising that surgical intervention is so rarely followed by intra ocular infection

The explanations of this must be that *Staph albus* usually is apathogenic and that the protective apparatus of the conjunctiva is rather efficient. The most important protective agents are lysozyme in the tears antibody leucocyte phagocytosis and competing bacteria

One may also wonder that staphylococci are not always present in the conjunctiva This may be due not only to the above factors but also to removal by transportation with the tears and with mucus *via* the mucous thread in the lower conjunctival fornix (*Norn* 1969 A)

The results of the present investigation suggest that the majority of staphylococci are situated in and round the hair root whereas relatively fewer bacteria are found at the tip of the hair

Pre operative cutting of the eyelashes therefore cannot be taken to reduce the number of bacteria

However if the lashes lie bare within the field of operation it may often be necessary to cut them for purposes of space

Summary

A total of 153 single eyelashes epilated from 33 eyes of 17 patients have been subjected to bacteriological examination

Table II
Resistance pattern of bacterial strains cultured from eyelashes

	number of strains	*penicil*	*sulpha*	*strepto*	*tetra*	*chloromyc*	*erythr*
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Staph albus from non antibiotic treated pts in per cent	42	81	83	19	40	38	0

We considered if our patient might suffer from optic neuritis as a manifestation of a demyelinating lesion Her normal vision and normal visual fields were to some extent against this assumption

Daroff & Lawton Smith (1965) reported on three patients with *optic neuritis* and normal visual acuity but field defects were present and the cases were unilateral as distinct from ours

Chamlin (1953) collected 100 cases of optic neuritis Among these the visual acuity was normal in 21% and only slightly impaired in another 16% All these patients revealed field defects although they were only small and of peripheral distribution in some cases *Unfortunately* the author did not state the frequency of papilloedema but it must have been present in some of the patients since he concluded This is corroborative evidence that the preservative of central visual acuity alone must not be used as a major criterion for differentiating optic neuritis from other conditions such as papilledema It appears from the paper that there were several bilateral cases of optic neuritis but the number is not stated

François (1956) discussed the differential diagnosis of *papillitis and choked disc* He reported six cases of papilloedema The visual acuity was normal but all the patients had field defects In one case the papilloedema was bilateral and the field defect in one eye was doubtful but as the patient had concurrent hypertension the findings are difficult to assess

Roper Hall (1958) reported five cases of optic disc oedema associated with normal visual fields and near normal visual acuity and absence of increased intracranial pressure He interpreted this combination as a *nutritive phenomenon* on the assumption that when the ratio of the arterial to the venous pressure in the retina is 3 2 instead of 3 1 this will result in malnutrition and hence oedema of the disc He expressed the view that this is the case in partial venous thrombosis malignant hypertension Guillain Barre s syndrome and hypotension occurring after head injury Even though it is not quite unlikely this explanation must be taken with some reserve as the assumption is of a purely hypothetical nature as long as the available measuring methods are relatively inaccurate

According to studies by *François* (1956) and *Chamlin* (1959) vitreous opacities suggest optic neuritis (papillitis) but not choked discs

As our patient had normal blood pressure hypertensive changes can be ruled out

Bilateral *central vein thrombosis* referable to hypertension and arteriosclerosis is not uncommon but in our case there was no evidence in favour of this diagnosis

Another diagnostic possibility was retinal vasculitis *Retinal vasculitis or periva culitis* is not a well defined disease entity It comprises retinal vascular lesions of widely different aetiology and morphology Thus *Ballentyne &*

Lumbar puncture revealed a pressure of 650 mm H_2O (sitting position) and 54 mg% protein leukocytes 114 spinal sugar normal

The neurological signs were aggravated during the next 6 weeks and several lumbar punctures showed unchanged conditions The patient was treated with corticotrophin which resulted in an improvement in the gait but the patient still had to walk with two sticks

Ophthalmological examination showed a visual acuity of 6/7 5 + 1 0 in the right eye and 6/10 + 1 0 in the left The position and direction of the eyes were normal and the ocular movements were unimpended in all directions No nystagmus or jerky ocular movements The corneal sensibility was normal The pupils were of equal size in maximal mydriasis

Slit lamp examination showed that the corneae were clear A fine aqueous flare was seen in the anterior chamber on both sides and numerous opacities of the vitreous were present Ophthalmoscopy revealed oedema and pronounced hyperaemia of both discs with a swelling of 1 dioptre The veins were very dark greatly dilated and tortuous with periphlebitis centrally and peripherally Colour sense normal field of vision 5/1000 red/white normal

An examination performed 5 days later showed haemorrhages at the margins of the discs and the ophthalmoscopic appearance was still characterised by considerable venous stasis Field of vision normal During the next few months the venous stasis decreased and the haemorrhages vitreous opacities and the aqueous flare gradually subsided

The patient returned for a check up examination 11 months after the onset of the disease The gait was now practically normal and the neurological manifestations had disappeared The visual acuity was 6/6 + 0 5 in both eyes Ophthalmoscopy showed well defined discs with a few newly formed vessels at the margins There was no vascular stasis but some residual periphlebitis was present Visual fields normal

Discussion

At the first examination of our patient the ophthalmoscopic findings were strongly suggestive of choked discs but the presence of a normal pressure on lumbar puncture weighed against a diagnosis of choked discs caused by a space occupying intracranial lesion The diffuse neurological symptoms with bilateral sensory and motor deficits were in facour of a disseminated disease

In his survey of the literature on *choked discs and spinal tumours* *Newman* (1958) reported some cases in which tumours of the cervical spine produced choked discs because of retrograde brain oedema In the present case the clinical picture and the normal cervical cord revealed by pneumo encephalography militated against the presence of such a tumour

Stapford (1951) reported a number of cases of supratentorial tumours associated with *choked discs and normal intracranial pressure* but his explanation viz obstructed venous drainage is not acceptable However there was no evidence in favour of such a tumour in our patient

We considered if our patient might suffer from *optic neuritis* as a manifestation of a demyelinating lesion. Her normal vision and normal visual fields were to some extent against this assumption.

Daroff & Lawton Smith (1965) reported on three patients with optic neuritis and normal visual acuity but field defects were present and the cases were unilateral as distinct from ours.

Chamlin (1953) collected 100 cases of optic neuritis. Among these the visual acuity was normal in 21% and only slightly impaired in another 16%. All these patients revealed field defects although they were only small and of peripheral distribution in some cases. Unfortunately the author did not state the frequency of papilloedema but it must have been present in some of the patients since he concluded "This is corroborative evidence that the preservative of central visual acuity alone must not be used as a major criterion for differentiating optic neuritis from other conditions such as papilledema". It appears from the paper that there were several bilateral cases of optic neuritis but the number is not stated.

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Michaelson (1937), *Duke-Elder* (1967) and others included Eales disease in which vitreous haemorrhages occur under this heading On the other hand *Sorsby* (1963) differentiated retinal vasculitis from Eales disease just because of the vitreous haemorrhages in the latter *Lyle & Wybar* (1961) occupy an intermediate position they divided vasculitis into two groups one with peripheral retinal changes and another characterised by changes in the central vein especially complete or partial thrombosis *Lyle & Wybar* (1961) reported a case in which there were peripheral changes in one eye and central changes in the other This should be suggestive of an *auto-immune process*

Miescher et al (1968) studied the immunological changes in the skin in vasculitis by immune fluorescence technique He concluded "Each phenomenon may serve as a control for the findings in other immune phenomena

Eales disease with large vitreous haemorrhages is very similar to a Schwartzmann phenomenon It is usually bilateral with a fairly great time lag for the occurrence in the second eye This points in the direction of an auto immune disease *Lyle & Wybar* (1961) published a total of seven cases of retinal vasculitis including two which were bilateral One of these was that mentioned above, the second showed changes mainly suggestive of thrombosis of the central retinal vein Only in the presence of macular haemorrhages did severe visual impairment occur None of these patients had neurological manifestations

Lonn & Hoyt (1966) published five cases of unilateral papilloedema with distinct signs of involvement of the central retinal vein the patients were otherwise healthy young men The authors expressed the view that the designation retinal vasculitis" is unnecessarily general and may comprise a number of different diseases and they suggested that a special group should be segregated viz cases characterised by papilloedema normal or near normal visual acuity normal visual field dilated veins and scattered peripheral haemorrhages and that this entity should be called *papillophlebitis* a term which seems adequate

Another problem faced in our case was the relationship between the uveitis and the neurological manifestations

First it must be emphasised that the eye is developed from all three germ layers Accordingly allergic disorders in all groups of tissue can result in similar processes in the eye as is seen for example in rheumatic diseases allergic skin disorders and many other groups of diseases Secondly it should be mentioned that the uvea and retina apparently contain identical antigens and it is therefore impossible to differentiate these two organs in allergic affections Owing to the intimate anatomical relationship between the uvea and retina an affection of one of the two organs will also often involve the other

Both from a clinical and an immunological point of view there is thus an intimate relation between uveitis and demyelinating processes in the central nervous system

Braak & Herwaarden (1933) published a survey in which they reported six cases of ophthalmo encephalomyelitis of their own and discussed the causes of the unquestionable relationship between demyelinating lesions in the central nervous system and pathological findings in the eye especially those localised in the vessels of the uvea and retina They expressed the view that the cause of this relationship is a combination of an infection and immunological processes

As distinct from those in the central nervous system the lesions of the eye are not of a permanent nature because the eye does not contain myelin sheaths the process is therefore arrested at the ocular vessels and does not result in permanent loss of function

In our patient periphlebitis was seen in several places along the retinal veins It is now generally recognised that this is a common finding in patients with multiple sclerosis It was first described by *Haarr* in 1951 and later by *Rucker* (1954) who observed it in 10 % of his patients *Moller & Hammerberg* (1963) reported that retinal periphlebitis is present in up to 20 % of patients with multiple sclerosis

In their paper of 1933 Braak & Herwaarden described ophthalmoscopic observations which must have been manifestations of retinal periphlebitis In 1965 Fog published histological studies of the eye and central nervous system in patients with multiple sclerosis He found that the retinal periphlebitis and the pathological vascular changes in the central nervous system are of the same nature and concluded From the point of view of pathological anatomy multiple sclerosis is a condition of periphlebitis cerebrospinalis and retinalis As encephalomyelitis is also a demyelinating lesion it is reasonable to assume that his conclusion also applies to this disease

Iridocyclitis is a condition which is not uncommon in patients with multiple sclerosis Thus *Tschabitscher et al* (1957) found this complication in 5 5 % of their patients *Haarr* (1961) reported that 4 5 % of his patients with iridocyclitis suffered from multiple sclerosis and *Bech* (1961) found multiple sclerosis in 4 % of his cases of chronic iridocyclitis These percentages are so high as compared with normal series that they must represent a significant difference

There are many points of resemblance between uveoretinal affections and demyelinating lesions in the central nervous system In the aetiology of these disorders we must consider both infectious factors particularly virus infections and the possibility of antigen antibody formation In addition auto immune factors must be taken into account and finally a patho anatomical comparison must be made

Pette & Pette (1963) *Ross et al* (1965) and *Wright et al* (1965) performed immunological studies on patients with multiple sclerosis and other demyelinating lesions There seems to be a certain agreement between the results of these

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Summary and Conclusions

The *purpose* of the study here was through a comparison of the available literature and the findings in the case reported above to find out if there is a common pathogenic basis for demyelinating lesions in the central nervous system and diseases of the uvea The reasons outlined below are in favour of the existence of such a relationship

1 The frequency of *simultaneous occurrence* of these diseases is so high that it must be significant and cannot be due to mere chance

2 Concurrent *development of these diseases can be induced experimentally* by the injection of a single causative agent

3 Good agreement exists between the experimental results obtained by neurologists and ophthalmologists *in the study of antigen antibody formation* and auto immunisation as factors in the pathogenesis of these disorders

4 As is well known both uveitis and demyelinating lesions occur simultaneously as complications of a number of common virus diseases such as measles and herpes zoster

5 *Signs of thrombotic processes in the central vein of the retina in both eyes* were observed in our patient with a demyelinating lesion This also shows the interdependence assumed in the theory that thrombosis of the small veins of the central nervous system may be the cause of demyelinating lesions

The reason why the term demyelinating lesion is used throughout this paper instead of a definite diagnosis within this group of diseases is that it could not be unquestionably determined if our patient suffered from disseminated encephalomyelitis or multiple sclerosis only the further course of the disease and particularly future seizures if any will reveal the exact diagnosis

The considerations set forth here must not be taken as proof of the theory of a common pathogenesis of the diseases in question but the case reported lends support to this theory since it revealed definite thrombotic processes in the venous system of the retina in a patient with a demyelinating disease

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authors and those obtained by *Agarval et al* (1963) in their studies of the aqueous humour in patients with uveitis

Boke (1968) advanced a theory of the auto immune process occurring in the uvea infection of the uvea leading in turn to uveitis production of uveotropic antibodies and finally, to auto immune uveitis This sequence represents a vi i ous circle and ultimately results in uveitis of the other eye This theory also ex plains the time lag not infrequently seen in the involvement of the second eye in bilateral chronic uveitis Thus *Bech* (1961) found that there was a time inter val of more than 12 months between the development of the disease in the two eyes in 20 % of 106 patients with chronic bilateral uveitis In experiments on pigs *Fog* & *Bardram* (1953) induced concurrent encephalitis and uveitis by in jection of homologous and heterologous brain extract

In the discussion of the relation between multiple sclerosis and uveitis it must be emphasised that the frequent finding of vitreous opacities in optic neuritis (papillitis) is an important sign in the differential diagnosis of this disease from choked discs since such opacities suggest involvement of that portion of the uvea which is adjacent to the optic nerve

As already mentioned *Fog* (1965) published a histological study on retinal periphlebitis in which he found a great similarity between the changes observed and those occurring along the veins in multiple sclerosis It must however be added that none of these changes are specific In multiple sclerosis thrombosis occurs in some of the veins in the affected portions of the cerebrum and spinal cord In older cases of uveitis histological examination will also disclose throm bosis of some of the veins In our case the ophthalmoscopic appearance was suggestive of venous thrombosis as evidenced by the choked discs considerable venous stasis and haemorrhages although these were not so extensive as is usually seen in central vein thrombosis Cases with a similar ophthalmoscopic appearance were described by *Lyle* & *Wybar* (1961) and *Lonn* & *Hoyt* (1966)

The neovascularisation observed in the vicinity of the discs in suggestive of the development of collaterals It must thus be presumed that the retinal circu lation was re established partly through the collaterals and partly by a re canalisation of the central vein That our patient regained normal vision after a transient impairment is in agreement with the observations of *Lyle* & *Wybar* (1961) and *Lonn* & *Hoyt* (1966)

In his study of central vein thrombosis *Brændstrup* (1950) found that it is principally in relatively young individuals that normal or near normal vision returns after the acute phase of the disease has passed off In our patient an acute catastrophe which is seen in so many cases of central vein thrombosis did not occur, and the relatively small number of haemorrhages suggests that the central vein thrombosis was only partial or that it developed so slowly that the compensatory factors operative in the re establishment of circulation went into action so early that the destructive processes in the retina were eliminated

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SKLERALINDENTATION UND PHOTOKOAGULATION

VON

F FANKHAUSER und W LOTMAR

1 Einleitung

Bei der Photokoagulation pra aquatorialer Netzhautveranderungen ist es eine gelaufige Erfahrung dass die Behandlung durch Skleral Indentation (SI) we sentlich erleichtert oder uberhaupt erst moglich wird Die Vorteile der SI die von Cibis (1) und Crignolo (2) ausfuhrlich gewurdigt wurden sind kurz die fol genden

a) Netzhautareale die normalerweise der Beobachtung nicht zuganglich sind werden in das Gesichtsfeld verschoben und konnen behandelt werden

b) Die Pulsenergie *die zur Erzielung einer klinisch ausreichenden* Photokoa gulation notwendig ist kann uber einem eingedellten Netzhautbezirk reduziert und damit die Strahlenbelastung der Augenmedien herabgesetzt werden

c) Die Bildqualitat im Beobachtungssystem wird verbessert und damit die Schnelligkeit und Sicherheit der Photokoagulation merklich erhoht

Bei der konventionellen Photokoagulation ohne Kontaktglas wird die SI auf einfache Weise durch stabchenformige Eindellungssporne erreicht Koaguliert man durch das Kontaktglas (Fankhauser & Lotmar (3)) so muss an diesem eine Eindellungsvorrichtung angebracht sein. Es stehen die Eindellungskontaktglaser n C llmann & Schmidt (4) der mit dem Goldmann Kontaktglas zusammen

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II Aufgabe

Im folgenden ist der Versuch unternommen worden, auf Grund von Strahlendurchrechnungen durch ein theoretisches Augenmodell bis zu hohen Werten des Gesichtswinkels angenähert quantitative Aussagen über die Wirkung der SI auf die optischen Verhältnisse bei der Photokoagulation zu gewinnen. Die Ergebnisse gelten dabei dem Sinne nach in gleicher Weise für die konventionelle Methode wie für die Koagulation durch das Kontaktglas von Goldmann.

Das zugrundegelegte Augenmodell wird an anderer Stelle eingehend beschrieben (Lotmar (9)). Die hier interessierenden Zusammenhänge sind im wesentlichen die Abhängigkeit der scheinbaren Pupillengrösse und des Auftreffwinkels auf der Netzhaut vom Gesichtswinkel des einfallenden Strahlenbündels. Abb. 2 erläutert die verwendeten Winkelbezeichnungen. Als Gesichtswinkel wird hier der Winkel zwischen der optischen Achse und dem einfallenden, durch die Pupillenmitte gehenden Hauptstrahl definiert. Die Strahlendurchrechnung liefert die zugehörigen Winkel der Hauptstrahlen nach Passieren der Linse, sodass bei bekannter Form des Augapfels die Auftreffwinkel auf der Netzhaut graphisch bestimmt werden können. Für die Form des Auges wurden die Angaben von Le Grand (10) übernommen. Aus der Durchrechnung weiterer Strahlen kann auch der Wert des bei schiefem Durchtritt verkürzt erscheinenden Pupillendurchmessers erhalten werden. Die Ergebnisse stimmen mit den von Jay (11) experimentell erhaltenen gut überein.

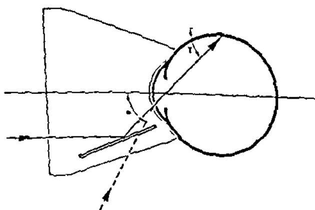


Abb. 2
Strahlengang und Bezeichnungen im System Auge plus Kontaktglas (mit Spiegel). α Gesichtswinkel, γ Auftreffwinkel. Gestrichelt: Einfallsrichtung des Hauptstrahls ohne Kontaktglas

wirkende Eindellungstrichter von Eisner (5, 6) und dessen Variation nach Linder (7) sowie das Eindellungskontaktglas von Fankhauser & Lotmar (8) zur Verfugung

Das mit dem Eindellungstrichter von Eisner versehene Goldmannglas hat sich in unseren Händen in der klinischen Praxis am besten bewahrt Mit der Version von Linder haben wir keine Erfahrung Das Kontaktglas von Fankhauser & Lotmar ist schematisch in Abb 1 dargestellt Es weist als einziges einen kontinuierlich verstellbaren Dorn auf bedarf aber noch weiterer Verbesserungen bis es klinisch auf breiter Front verwendet werden kann

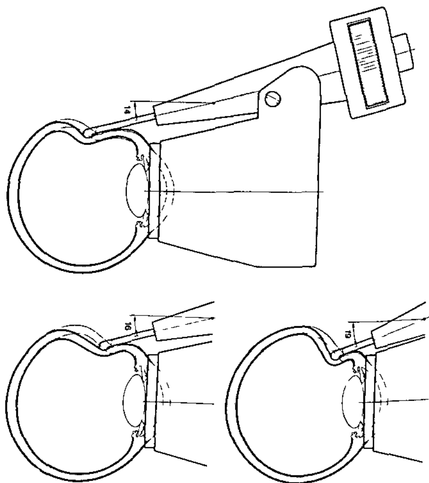


Abb 1

Schematische Darstellung der Eindellung durch den beweglichen Dorn des Kontaktglases nach Fankhauser & Lotmar fur drei verschiedene Neigungswinkel und je zwei Ausfahr Stellungen Starke der Eindellung ca 3 8 bzw 2 5 mm

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* Zu beziehen bei Firma E Huber Stockli Mechan Werkstatte Seftigenstr 71 CH 3123 Belp

II Aufgabe

Im folgenden ist der Versuch unternommen worden auf Grund von Strahlen durchrechnungen durch ein theoretisches Augenmodell bis zu hohen Werten des Gesichtswinkels angenahert quantitative Aussagen uber die Wirkung der Sf auf die optischen Verhaltnisse bei der Photokoagulation zu gewinnen Die Er gebnisse gelten dabei dem Sinne nach in gleicher Weise fur die konventionelle Methode wie fur die Koagulation durch das Kontaktglas von Goldmann

Das zugrundegelegte Augenmodell wird an anderer Stelle eingehend be schrieben (Lotmar (9)) Die hier interessierenden Zusammenhange sind im we sentlichen die Abhangigkeit der scheinbaren Pupillengrosse und des Auftreff winkels auf der Netzhaut vom Gesichtswinkel des einfallenden Strahlenbündels Abb 2 erlautert die verwendeten Winkelbezeichnungen Als Gesichtswinkel wird hier der Winkel zwischen der optischen Achse und dem einfallenden durch die Pupillenmitte gehenden Hauptstrahl definiert Die Strahlendurch rechnung liefert die zugehorigen Winkel der Hauptstrahlen nach Passieren der Linse sodass bei bekannter Form des Augapfels die Auftreffwinkel auf der Netzhaut graphisch bestimmt werden konnen Fur die Form des Auges wurden die Angaben von Le Grand (10) ubernommen Aus der Durchrechnung weiterer Strahlen kann auch der Wert des bei schiefem Durchtritt verkurzt erscheinen den Pupillendurchmessers erhalten werden Die Ergebnisse stimmen mit den von Jay (11) experimentell erhaltenen gut uberein

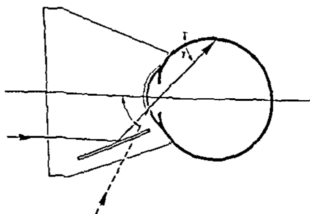


Abb 2
Strahlengang und Bezeichnungen im System Auge plus Kontaktglas (mit Spiegel) α Ge htswink l   Auftreffw nkel Gestrichelt Einfallsrichtung des Hauptstrahls ohne Kontaktglas

Die Form des Augapfels bei Eindellung (Abb 1) wurde nach Plausibilitats Ueberlegungen dargestellt Die Bestimmung des Auftreffwinkels sowie die An nahme daruber welcher Punkt der nicht eingedellten Bulbuswand sich auf der Kuppe des Eindelldorns befindet ist daher mit einiger Unsicherheit behaftet Die im folgenden gegebenen diesbezüglichen Kurven sind nur als halb quan titativ zu betrachten und sollen eine erste Annaherung darstellen

III Die verschiedenen Wirkungen der Eindellung

1 Scheinbarer Pupillendurchmesser

Die Kurve der Abb 3 gibt an um wieviel sich der Gesichtswinkel α andert, wenn eine Stelle der Netzhaut um 2 5 mm eingedellt wird Diese Aenderung be tragt beispielsweise für diejenige Stelle welche ohne Eindellung einem Ge sichtswinkel von 90° entspricht ca 19° d h dieselbe Stelle wird nach Eindel lung von dem unter 71° einfallenden Bündel getroffen In Abb 4 ist dargestellt, wie sich diese Aenderung bezuglich der für die Koagulation nutzbaren kleinen Pupillenachse auswirkt Während Kurve (a) die Pupillenbreite fur das normale Auge als Funktion des Gesichtswinkels angibt wobei ein Durchmesser von 8 mm angenommen wurde zeigt Kurve (b) die Breite fur die entsprechenden ein gedellten Netzhautstellen Man sieht dass beispielsweise bei 90° Gesichtswinkel die Breite ohne Eindellung 1 5 mm betragt bei Eindellung der betreffenden Stelle jedoch 3 7 mm was wie es sein muss dem Wert fur den Einfallswinkel 71° der Kurve (a) entspricht Da die Energie eines auf die Netzhaut fokussierten

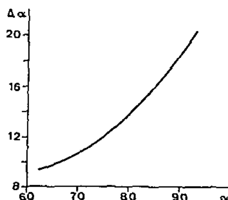


Abb 3

Effektive Verminderung des Gesichtswinkels auf einer um 2 5 mm eingedellten Netz hautstelle die ohne Eindellung von dem unter dem Winkel α (Abszisse) einfallenden Hauptstrahl getroffen wird

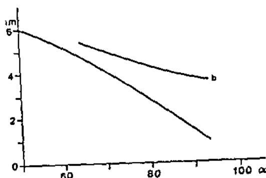


Abb 4

Kleine Achse der elliptischen Pupille in Funktion des Gesichtswinkels Kurve a Fur nicht eingedelltes Auge und Pupillendurchmesser von 8 mm (nach Jay) Kurve b Fur die entsprechenden Netzhautstellen bei Eindellung um 2 5 mm

Koagulationsbundels von kreisformigem Querschnitt quadratisch mit seinem Durchmesser in der Pupille zunimmt so entsprechen die in diesem Beispiel an gegebenen Zahlen einem Energiegewinn um das Sechsfache

2. Verringerung des Abstands der Netzhaut von der Pupille

Wie aus Abb 1 unmittelbar anschaulich hervorgeht kommt eine eingedellte Netzhautstelle auf dem sie treffenden Hauptstrahls wesentlich naher zur Pu pille zu liegen als diejenige Stelle welche vom selben Hauptstrahl ohne Ein dellung erreicht wird Ein auf die eingedellte Stelle fokussiertes durch die Pu pille im Querschnitt begrenztes Koagulationslichtbundel weist also einen gros seren Kegelwinkel d h eine hohere numerische Apertur auf als ohne Eindel lung Da die damit verbundene Energiesteigerung im Focus ebenfalls quadra tisch mit der Abstandsverminderung wachst ist auch dieser Effekt sehr wirk sam Dabei ist zu beachten dass bei der bisher ublichen Art der Koagulation mit parallel ins Auge fallendem Strahlenbundel sammelnde Vorsatzlinsen ver wendet werden sollten da ja sonst eine Defokussierung auftritt welche den erwarteten Energiegewinn zu nichte macht Bei der Koagulation durch das Kon taktglas sind dagegen keine Zusatzlinsen erforderlich indem durch Fuhrung der Optik nachfokussiert werden kann Im ubrigen kann naturlich die Moglich keit einen Lichtkegel grosserer Apertur durch die Pupille zu bringen bei be reits genugender Energie auch dahin ausgenutzt werden dass man die Aper tur nicht vergrossert dafur aber eine gewisse Bewegungsfreiheit in der Pu pille gewinnt was bei der stets mehr oder weniger vorhandenen Instabilitat des Systems Arzt Apparat Patient sehr wunschenswert ist

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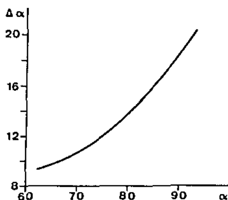


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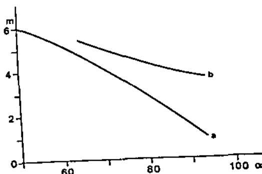


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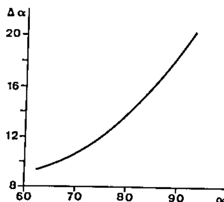


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Effektive Verminderung des Gesichtswinkels auf einer um 2 5 mm eingedellten Netzhautstelle die ohne Eindellung von dem unter dem Winkel α (Abszisse) einfallenden Hauptstrahl getroffen wird

ung der Zirkulation durch Eindellen keine Rolle. Beim *Arbeiten mit* kontinuierlichem Xenonbogen, wo die Pulsdauer in der Grossenordnung von 1 sec liegt, wird dagegen dieser Einfluss merkbar sein, d. h. die Eindellung wird den Wirkungsgrad der Koagulation etwas erhohen.

5. Gute der Abbildung

Die nach der Peripherie hin zunehmende Bildverschlechterung bei ophthalmoskopischer Beobachtung ist bekannt und wird durch die Strahlendurchrechnungen bestatigt. Sie ist auch bei Verwendung des Kontaktglases noch wahrzunehmen, allerdingst erst bei wesentlich hoheren Werten des Gesichtswinkels (ungefahr ab 80°). Was fur die mit relativ kleinen Bundel Aperturen arbeitende Beobachtung gilt, wirkt sich in noch wesentlich hoherem Masse fur Koagulationsbundel mit grosserer Apertur aus. Bezuglich Bildgute sowohl der Beobachtung wie der Strahlenvereinigung des Koagulationsbundels wird also die Eindellung gerade in der aussersten Peripherie von besonders hoher Wirkung sein, was durch die Erfahrung bestatigt wird.

Zusammenfassend kann gesagt werden, dass das Ansteigen des Wirkungsgrades der Photokoagulation mit zunehmender Skleral Indentation aus klinischen Erfahrungen zwar bekannt ist. Legt man sich jedoch die Frage vor, wie die Koagulationstechnik weiter verbessert werden konnte, so ist eine Kenntnis der einzelnen mitwirkenden Faktoren von einiger Bedeutung. Es sollte hier versucht werden, dazu in Bezug auf die Indentation einen Beitrag zu leisten.

Die Zeichnungen stammen von Peter Schneider

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2 *C .. I .* Ophthalmoscopy and other methods of examination in Controversial Aspects of the Management of Retinal Detachment Ed Schepens C L and Regan C D J Little Brown and Co (1965) pp 7 11

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6 *F .. r C* Zusatztrichter zum 3 Spiegel Kontaktglas mit verschieblichem Indentator .. les Arch Ophthal 1 8 183 186 (1969)

3 Auftreffwinkel

Kurve (a) von Abb 5 stellt den Auftreffwinkel des Hauptstrahls auf der Netzhaut bei nicht eingedelltem Auge dar Dieser Winkel betragt zwar beispielsweise fur einen Gesichtswinkel von 90° nur noch 38° jedoch ist die diesem Wert entsprechende Abnahme der Energiedichte eines auf die Netzhaut projizierten Koagulationsflecks nicht allzu drastisch namlich rund 40 % Durch Eindellung steigt der Auftreffwinkel wesentlich an (Kurve b) sodass namentlich gegen die ausserste Peripherie dieser Verlust nahezu vollstandig aufgeholt werden kann

Andererseits ist zu beachten dass bei schragem Lichteinfall die Dicke der durchlaufenen Netzhautschichten verlangert erscheint Die totale Absorption von Strahlung im Pigmentepithel welche fur die Koagulationswirkung massgebend ist nimmt daher zu Dieser Effekt kompensiert teilweise die oben besprochene Abnahme der Energiedichte Im ganzen durfte also die Grosse des Auftreffwinkels fur die Photokoagulation eher von untergeordneter Bedeutung sein

4 Kompression der Chorioidea

Wie Geeraets et al (12) gezeigt haben ist die Warmeableitung aus dem Koagulationsfleck durch den Blutstrom in der Chorioidea fur Pulszeiten unter 0 ? sec zu vernachlässigen Fur die Koagulation mit gepulsten Laserquellen deren Pulsdauer in der Grossenordnung von 1 msec liegt spielt daher die Unterbin

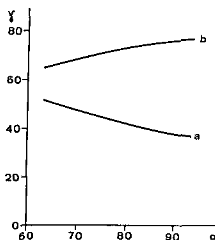


Abb 5

Auftreffwinkel γ in Funktion des Gesichtswinkels (a) ohne Eindellung (b) bei Eindellung der entsprechenden Netzhautstellen um 2 5 mm

Universitäts Augenklinik Bern (Direktor Prof Dr P Niesel)

SKLERALINDENTATION UND PERZEPTION

VON

F FANKHAUSER

I Einfuehrung

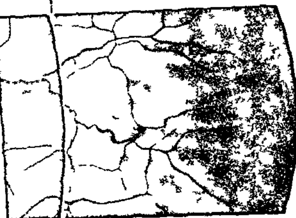
Wir haben kurzlich den Prototyp eines Eindellungskontaktglases beschrieben (1) und (2) dessen Eindellungssporn sich bezuglich Lange und Inklination relativ zum *Augapfel* wahrend der Beobachtung durch das *Kontaksglas* kontinuierlich verstellen lasst und das gestattet eine vom vordern Ende der Pars plana bis zum Aequator bulbi reichende Skleralindentation (SI) zu erzeugen

Es ist das Ziel der vorliegenden Arbeit die Wirkungsweise dieses Kontaktglases an zwei ausgewahlten Fallen zu demonstrieren

Im zweiten Teil dieser Arbeit werden wir uns mit den Sehmechanismen beschaftigen die der Wahrnehmung und Erkennung in der Biomikroskopie im allgemeinen und der Indentations Biomikroskopie im speziellen zu Grunde liegen Die Frage *warum* wir ein bestimmtes Phaenomen beobachten ist von ebenso grosser Wichtigkeit wie die Beschreibung dessen *was* wir sehen Nicht nur gewinnen wir dadurch einen Einblick in die optischen und biologischen Grundlagen des menschlichen Auges die der Perzeption zu Grunde liegen sondern wir werden in gleichem Masse zu apparativen Verbesserungen angeregt

Eingegangen am 2 Juli 1969
This investigation was supported by a Grant to the University of Bern Number NB 03638 04 from the NINDB National Institutes of Health Bethesda Maryland USA

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Figur 1
Netzhautbezirk zwischen Aequator und Ora serrata
I ohne Skleralindentation
II mit Skleralindentation
III Ora serrata naher Netzhautbezirk im Profil mit Skleralindentation
Nahere Erlauterungen im Text.









Figur 9
Netzhautbe rk in der Gegend des Aequators bulbi I ohne Skleraleindellung II mit Skleraleindellung Nahere Erlauterungen im Text

Die Wirkung des neuen Kontaktglases soll an zwei Fallen mit verschiedenem Schwierigkeitsgrad demonstriert werden Fall 1 zeigt die Eindellwirkung bei wenig komplizierten Verhältnissen Den einzigen wesentlichen Storfaktor stellt hier vermehrtes Streulicht dar Fall 2 zeigt ein Maximum an Komplexitat und interpretativen Schwierigkeiten Die zur Identifikation fuhrenden Teilmechanismen sind aus dem Gesamteindruck oft nicht eindeutig isolierbar In anderen Fällen scheint der dominante zur Wahrnehmung fuhrende Wirkungsmechanismus in die Augen zu springen Wo dies zutraf wurde bei der Beschreibung der Falle ausdrucklich darauf verwiesen Da die Phaenomene in Kapitel IV genauer erläutert sind werden sie erst spater wirklich verstandlich werden

Fall 1

Ein 57 jähriger Mann wurde am 4 7 1968 wegen einer beinahe totalen Amotio retinae o s in die Augenklinik Bern aufgenommen Eine genaue Untersuchung des Augenhintergrundes ergab verdächtige Stellen bei 11 h in Oranahe Der Einblick war wegen einer geringfügigen Kerntrübung nicht besonders gut Eine am 8 7 1968 durchgeführte Diathermokoagulation der verdachtigen Stellen sowie eine Umschlingung des Bulbus mit einem Skleraband und Ablassen der retroretinalen Flüssigkeit brachte eine sofortige Wiederanlegung Die fruher als verdachtig angesehenen Herde konnten nun mit Sicherheit als Ursache der Netzhautablosung eruiert werden indem sich in deren unmittelbarer Umgebung anterior des Umschlingungsbandes etwas subretinale Flussigkeit ansammelte Die umschriebenen Flussigkeitspolster wurden mit einer Photokoagulationsbarriere eingekreist Schliesslich wurden Photokoagulate direkt auf die Läsionen gegeben

Bei der Untersuchung des rechten Auges fand sich eine geringfugige bis massig stark entwickelte Kerntrubung Bei stark schrägem Einblick storte das durch die Trubung erzeugte Streulicht deutlich Das Gesichtsfeld betrachtet über den um 67° gegen die plane Vorderflache geneigten Spiegel des Dreispiegelglases von Goldmann reichte bis in die Nahe der Ora serrata Wir beschränken uns hier auf die Beschreibung eines schmalen Netzhautsektors bei 9 h der ungefahr vom Aequator bis in die Nähe der Ora serrata reichte (Figur 1)

Die subjektive Beurteilung ohne SI ergab den Eindruck guter Bildscharfe in posterior anteriorer Richtung bis zu einer bestimmten Stelle des Fundus zwischen Aequator und Ora serrata An einem ziemlich gut definierten Punkt (1a) hatte man den Eindruck beginnender Bildunscharfe die sich in anteriorer Richtung (Pfeil Figur 1 I) verstärkte wobei sich in diesem Gebiet die Strukturen zunehmend auflosten Die Ora serrata ist in dem Bild nicht dargestellt Sie

hervor (Optischer Schnitt der Retina bei III 5) Ein drittes Loch war im Profil mit dem inserierenden Glaskorper *unter hohem* Kontrast gegen den defokussierten dunkelblauen Hintergrund (III 4) sehr scharf erkennbar

Fall 9

Ein 56 jahriger Mann wurde am 26 6 1968 wegen einer Netzhautablosung mit Lochbildung rechts in die Augenklinik Bern eingewiesen Die Netzhautablosung konnte mit Diathermie und einem eindellenden Eingriff geheilt werden Am 22 8 1968 wurde der Patient mit einem Recidiv wieder aufgenommen *wobei* sich die Ablosung auf den temporalen oberen und teilweise temporal unteren Quadranten beschrankte Ein grosses Hufeisenloch wurde bei *11 h etwas poste* rior des Aequators gefunden eine Gruppe mit kleineren Lochern fand sich bei 10 h und bei 9 h wurde ein weiteres Hufeisenloch entdeckt Die ganze Peripherie zeigte degenerative Veranderungen auf die hier nicht naher eingegangen wird Die Locher wurden mit Diathermie getroffen ferner wurde eine Skleratasche von 8 45 bis 11 15 h angelegt deren Grund mit stumpfer Diathermie behandelt und schliesslich mit konservierter Sklera ausgestopft wurde Im postoperativen Verlauf erfolgte prompte Wiederanlegung

Am 5 8 und 10 10 1968 wurde die Umgebung des Loches bei 9 h mit dem Eindellungskontaktglas genauer untersucht Dabei zeigten sich eine grosse Zahl von Storfaktoren die die Erkennung wichtiger Einzelheiten stark behinderten

Figur 9 I gibt die Verhaltnisse ohne Figur 2 II die Situation mit Eindellung wieder

Die Aufsicht auf die *Figuren 9 I und II (bis 2 rechter Bildrand) gibt den* unverzerrten Eindruck wieder Der Schnitt der Schichten bis und mit (5) ist *in dem Sinne* halbschematisch als die *naturlichen Proportionen* nicht eingehalten wurden Zwischen (4) und (5) wurden die tiefen Chorioidalgefasse die (*vom Atrophiebezirk unterhalb* des Deckels abgesehen) nicht sichtbar waren sinngemass erganzt Der Lockdeckel ist bei (a) sichtbar Das Loch selber ist *nicht mehr sichtbar und ist durch* reaktive Pigmentproliferationen verdeckt. Links unterhalb des Deckels beobachtete man die obenerwahnte atrophische *Zone in der nur* einige Chorioidalgefasse erhalten sind Weiter findet sich eine Blutung bei (b) die im optischen Schnitt in die Retina lokalisiert werden konnte *Daran* schliesst sich eine atrophische Zone (c) mit lockerer Ausstreuung von polymorphem Pigment an das ebenfalls intraretinal liegt Es folgt nach *unten ein Gebiet* das durch eine unregelmassige Oberflache charakterisiert ist (d) Die streifigen Oberflachenirregularitaten (die einen weiss rotlichen Farb*ton hatten)* waren gegen das atrophische Gebiet ausgerichtet was auf Zug

darf bei etwa (3) der Figur 1 I und II angenommen werden Ueber allen Arealen hatte man den Eindruck uniformer und homogener Dicke und Verteilung des Pigmentepithels Die Netzhautoberflache war regelmassig (glatter Oberflächenstreifen 1) Die Einfallsrichtung des Beleuchtungsbundels ist in Figur 1 durch einen dicken horizontalen Pfeil angedeutet Figur 1 II gibt die gleichen Abschnitte bei Eindellung wieder Diese ging so vor sich dass der Eindellungsdorn mit zunehmender Steilheit relativ zur optischen Achse gegen posterior verschoben wurde Diese verschiedenen Eindellungspositionen wurden in der Figur in einen Eindruck verarbeitet wobei der Eindellungsdorn in seiner Endposition dargestellt ist Das Eindellungsbild der an die Ora serrata angrenzenden Netzhaut ist in Figur 1 III dargestellt Die Eindellungsbilder 1 II und III ergaben foldende wesentlichen Unterschiede relativ zu Figur 1 I

1 Ueber dem *ganzen* einsehbaren Gebiet herrschte der subjektive Eindruck der Bildscharfe

2 Die Abblassung des Fundusrot uber dem Eindellungsgebiet war ausgesprochen Das Rot hatte einem gelblichen Farbton Platz gemacht Die grossen Chorioidalgefasse waren noch sichtbar Sie erschienen verdunnt und der sie auszeichnende rote Farbton relativ zu I entsattigt

3 Gegen den abgeblassten Hintergrund trat Struktur und Verteilung des chorioidalen Pigmentes ausserordentlich deutlich hervor und feinste Pigmentkorner konnten ohne Schwierigkeiten erkannt werden Aus Figur I hatte man geschlossen dass sich das chorioidale Pigment homogen auf die Intervaskularen Bezirke verteile

Es ist mit grosser Wahrscheinlichkeit anzunehmen dass die Verbesserung des Auflosungsvermogens durch eine Verbesserung der Bildqualitat und durch eine Umwandlung der Farbkontraste in Schwarz Weiss Kontraste infolge Kompression der Chorioidea zu Stande kam

4 Die Glaskorperstruktur im retrolentalen Raum (2b) war leicht beurteilbar ebenso wie die Insertion der Glaskorperbasis an der Retina die einzelne feine Verdickungen an der Netzhautoberflache zeigte (2c) die sich als feine Streifen gegen die Ora serrata fortsetzten (2a deutet den Linsenrand mit dem Abspaltungsstreifen an)

5 Bemerkenswerterweise erschienen die typische chorioidale Pigmentstruktur und feinste Netzhautgefasse nun auch in der Zone die ohne SI (Figur I) als subjektiv scharf jedoch als homogen und frei von feinsten Netzhautgefassen beurteilt worden war

Subjektive Bildscharfe ist somit kein zuverlassiges Kriterium fur das Auflosungsvermogen

6 Die an die Ora serrata angrenzende Retina erschien in III vollig scharf Ihre Farbe war in Schragprojektion grau weiss wobei das Pigment der Chorioidea kornig durchschimmerte Gegen den nicht eingedellten rotlichen Hintergrund traten in den ausgedehnten Blessig Iwanowschen Cysten zwei ovale Locher

III Wahrnehmung Erkennung und Identifikation in der Biomikroskopie

Wahrnehmung ist bekanntlich eine notwendige aber nicht hinreichende Voraussetzung zur Erkennung und Identifikation *einer bestimmten* Struktur Wir werden diese beiden Prozesse aus diesem Grunde getrennt behandeln

1 Wahrnehmung in der Biomikroskopie

Man darf als allgemein bekannt voraussetzen dass die Sichtbarkeit eines stationaren *Objektes von der Helligkeit* des Hintergrundes auf dem es erscheint von seiner Form seiner angularen Grosse ferner von seinem Helligkeits und Farbkontrast abhangt

Allgemein gilt je grosser die Helligkeitsdifferenz zwischen Objekt und Hintergrund ist umso besser wird das Objekt wahrgenommen wobei wir hier einen uniformen Hintergrund voraussetzen

Diese Aussage lasst sich auf mikroskopische Bilder ubertragen Da alle Dimensionen eines Objektes linear vergrossert werden hangt die durch das Mikroskop wahrgenommene Flache eines Objektes A mit der Vergrosserung M und der wirklichen Flache A des Objektes durch die Beziehung

$$A = A\ M^2 \qquad (1)$$

zusammen

Kleine nicht sichtbare Objekte konnen somit wenn sie geeignet vergrossert werden durch Helligkeitssummation wahrgenommen werden

Die durch die Vergrosserung bedingte Verbesserung der Wahrnehmung erreicht in der Biomikroskopie jedoch sehr bald einen Grenzwert der erfahrungsgemass bei klaren Medien etwa bei einer 20 fachen Vergrosserung liegt Starkere Vergrosserungen bringen infolge der durch Vibrationen erzeugten Bildunscharfe und der zunehmenden Gesichtsfeldeinengung im allgemeinen keinen Gewinn Sind die Medien trube so wird die Vergrosserung in dem Masse weniger wirksam als die Turbiditat der Medien zunimmt

Es ist wichtig zu wissen dass die Sichtbarkeit von Objekten gleichen Flacheninhaltes fur kreisformige *Objekte immer am besten ist (3) und (4) Der* wichtigste Faktor der die Sichtbarkeit beeinflusst ist der durch den Beobachter wahrgenommene scheinbare Bildkontrast C Dieser setzt sich aus zwei Komponenten zusammen Die eine ist der scheinbare Helligkeitskontrast C_b und die andere der scheinbare Farbkontrast C die bei der Erkennung von farbigen Objekten stets zusammenwirken Der Beitrag von C_{ca} und C_b fur die Erkennung nimmt die allgemeine Form an

$$C \quad (C_i{}^2 + C\ {}^2) \qquad (2)$$

wirkung durch das Narbenareal schliessen lasst Diese Interpretation wird da durch gestutzt dass durch SI (Aenderung der Spannungsverteilung in der Retina) die Irregularitaten ihre Ausrichtung verloren und einer unregelmassigen hockerigen Oberflache Platz machten (Figur 2 II) Ohne Eindellung waren die Netzhautunebenheiten wegen der durch die Ueberlagerung mit polymorphen Glaskorpertrubungen erzeugten Tarnung nicht erkennbar Durch Hin und Herbewegen des Dornes wurden die Glaskorpertrubungen und die Netzhaut irregularitaten sowie die darunter liegenden Strukturen als schichtweise angeordnete separate Strukturen unterscheidbar Die Erkennung erfolgte hier offensichtlich auf Grund der durch den Dorn induzierten Bewegungsperspektive Im Streifen (1) bis (1) ist durch den Kunstler versucht worden die Storwirkung der Glaskorpertrübungen auf die darunterliegenden Strukturen darzustellen Ueber den ubrigen Bildpartien wurde der getrubte Glaskorper mit seinen Opazitaten weggelassen (1) zeigt den optischen Schnitt durch den Glaskorper (2) den Schnitt durch die Retina Man erkennt dass die faserigen und klumpigen Elemente kurz vor der Netzhaut an einer wenig scharfen Membran enden die in der unteren Halfte der Figuren 2 I und II feine Faserzuge zur Netzhaut sendet

In Figur 2 I sieht man dass von den oberflachlichen Chorioidalgefassen nur diejenigen deutlich hervortreten die perpendikular oder in einem grossen Winkel gegen die Streifenzeichnung der Netzhaut verlaufen Parallel zur Streifenzeichnung laufende Chorioidalgefasse sind nur mit grosser Muhe erkennbar Eine Deutungsmoglichkeit fur dieses Phaenomen besteht darin dass der Tarneffekt *einer uberlagernden Struktur bei paralleler Ausrichtung* zur uberlagerten Struktus viel ausgeprägter sein kann

Die genaue Konfiguration der Oberflachenirregularitaten wird im Profil durch SI in Figur 2 II deutlich Bei der Indentationsbedingten seitlichen Betrachtungsrichtung nimmt die Retina durch Vergrosserung der scheinbaren Schichtdicke einen grauen Ton an und es gelingt ein System bestehend aus hochgradig verdunnten Stellen auszumachen (e) die sobald der Eindellungsdruck *etwas nachlasst sofort ausgesprochen rot gegen die* graue Netzhaut erscheinen Der Schnitt mit dem dunnen optischen Spalt (2) zeigt durch Spalttransposition dass die drei Verdunnungen am unteren Bildrand bereits durchgerissen sind und Locher darstellen Man beachte die drei zusammenhangenden Deckel die sich auf die Netzhautoberflache geklappt haben Wenn wir die Figuren 2 I und II miteinander vergleichen wird es offensichtlich dass wir die drei Locher wegen der ungunstigen Beobachtungsbedingungen ohne Eindellung *ubersehen hatten*

Schicht (2) bis (3) zeigt die Retina und Schicht (3) bis (5) die Chorioidea im optischen Schnitt Die Vernarbungen im oberen Teil des Bildes in der Nahe der Deckelinsertion wurden blaulich wiedergegeben da sie im kurzwelligen Blaulicht blaulich weisslich fluoreszierten

Bei extrem schragem Strahlengang nimmt die CR sehr niedrige Werte an Durch den Einsatz des Kontaktglases wird die CR jedoch wieder angehoben wie fruher auseinandergesetzt worden ist (1)

SI fuhrt zu einer weiteren Verbesserung der CR indem das eingedellte Netz hautareal gegen die optische Achse zu verschoben und dort unter einem klei neren Gesichtswinkel mit einer besseren CR beobachtet werden kann

Die Anwendung des Kontaktglases und SI fuhren somit synergistisch zu ei ner Erhohung der scheinbaren Helligkeits und Farbkontraste

Andererseits fuhrt Streulicht zu einer Reduktion der scheinbaren Kontraste und damit zu einem Abfall der CR

2. Verminderung des Streulichtes durch SI

Die Verminderung des Streulichtes im Beobachtungssystem und damit die Ver besserung der Bildqualitat kann auf zwei Arten zustandekommen

a) Durch die Eindellung wird die kleine Achse der in Schragprojektion ellip tisch deformierten Pupille infolge des verminderten Gesichtswinkels effektiv vergrossert *Bei der Beobachtung der seitlichen* Fundusabschnitte fallen der Beobachtungsstrahl sowie der Beleuchtungsstrahl (bei monokularen Instrumen ten) oder die beiden Beobachtungsstrahlen sowie der Beleuchtungsstrahl (bei binokularen stereoskopischen Instrumenten) in die kleine Achse der elliptisch deformierten Pupille Wir wissen dass das in das Beobachtungssystem ruckge strahlte Streulicht in dem Masse abnimmt als es uns gelingt den Beleuchtungs und Beobachtungsstrahlengang in der Pupille und den Medien zu trennen

Dies wird bei einigen Instrumenten durch Anlage des Beleuchtungssystems in der Art erreicht dass der Beleuchtungsstrahl uber oder unter die beiden Beo bachtungsstrahlen *zu liegen kommt* Bei *einem in der Pupille frei verschiebba* ren Beleuchtungsstrahl der Instrumente dieser Klasse wird dieser in der grossen Achse der elliptisch deformierten Pupille und so weit wie moglich von den Beobachtungsstrahlen weggeschoben

Wenn die apparativen Voraussetzungen fur die Verschiebbarkeit des Be leuchtungsstrahles fehlen so wird die Voraussetzung fur eine bessere raumliche Trennung durch die Eindellung dadurch geschaffen dass der kleine Pupillen durchmesser effektiv vergrossert wird Eine *quantitative Abschatzung dieses* Effektes wurde an anderer Stelle gegeben (?)

b) Von der Vergrosserung des *nutzbaren Pupillendurchmessers* abgesehen ist zu beachten das durch die Eindellung die betreffende Netzhautpartie nicht *nur gegen das Rotationszentrum* des Auges verschoben wird Eine Komponente der Eindellrichtung ist gegen die Pupille gerichtet wodurch der optische Weg des Beobachtungs und Beleuchtungsstrahles im Auge abnimmt Bei starker Turbiditat wird durch diese Verminderung der Schichtdicke und die damit ver

Sobald der scheinbare Kontrast C_a unter einen kritischen Wert sinkt der durch die Kontrastempfindlichkeit des Beobachters gegeben ist wird das Objekt nicht mehr wahrgenommen

Zur Beurteilung der Wahrnehmbarkeit eines Objektes braucht jetzt nur noch der Zusammenhang zwischen dem scheinbaren Kontrast C_a und dem Objekt kontrast C_o hergestellt zu werden

Dieser Zusammenhang wird durch die Formel (3) gegeben

$$CR = C_a \quad 100/C_o \tag{3}$$

worin CR die Kontrastrendite in Prozent bedeutet Die CR ist ein Mass fur die Gute eines gegebenen optischen Systems

2 Erkennung und Identifikation

Die Erkennung und Identifikation bestimmter Strukturen in der Biomikroskopie wird in vielen Fällen nicht so sehr dadurch erschwert dass Strukturen als ganze oder in Strukturen eingebettete Einzelobjekte nicht wahrgenommen wurden sondern dadurch dass sie in einer komplexen Umgebung liegen in der sie nicht erkannt werden und durch Tarnung verschwinden Die sich uberlagernden Schichten der Netzhaut und Aderhaut und oft auch des Glaskorpers die wieder aus zahlreichen Einzelelementen bestehen bilden einen Hintergrund der aus multiplen sich uberschneidenden Strukturelementen besteht und die Identifikation pathologischer Veranderungen in vielen Fallen erschwert oder verunmoglicht

Es ist wohlbekannt dass die Wahrscheinlichkeit ein Einzelobjekt als solches zu erkennen in dem Masse abnimmt als die Gesamtheit der nicht relevanten das Objekt einbettenden übrigen Strukturelemente zusammengedrangt wird (5) (6) und (7) Die Erfahrung lehrt dass bei diagnostischen Schwierigkeiten die auf diesem Tarneffekt beruhen durch SI oft Erkennung moglich ist

IV Die Wirkungsweise der Skleralindentation

Die Wirkung der SI besteht darin die optischen Voraussetzungen im unberuhrten Auge so zu verandern dass die Erkennung und/oder Wahrnehmung schwer erkennbarer Strukturen verbessert oder uberhaupt erst moglich wird

1 Das Zusammenwirken von SI und Kontaktglas Biomikroskopie

Das dioptrische System des Auges ist dadurch charakterisiert dass die CR umso mehr abnimmt je schrager das System vom Strahlengang durchlaufen wird

Bei extrem schragem Strahlengang nimmt die CR sehr niedrige Werte an Durch den Einsatz des Kontaktglases wird die CR jedoch wieder angehoben wie fruher auseinandergesetzt worden ist (1)

SI fuhrt zu einer weiteren Verbesserung der CR indem das eingedellte Netzhautareal gegen die optische Achse zu verschoben und dort unter einem kleineren Gesichtswinkel mit einer besseren CR beobachtet werden kann

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Dies wird bei einigen Instrumenten durch Anlage des Beleuchtungssystems in der Art erreicht dass der Beleuchtungsstrahl uber oder unter die beiden Beobachtungsstrahlen zu liegen kommt Bei einem in der Pupille frei verschiebbaren Beleuchtungsstrahl der Instrumente dieser Klasse wird dieser in der grossen Achse der elliptisch deformierten Pupille und so weit wie moglich von den Beobachtungsstrahlen weggeschoben

Wenn die apparativen Voraussetzungen fur die Verschiebbarkeit des Beleuchtungsstrahles fehlen so wird die Voraussetzung fur eine bessere raumliche Trennung durch die Eindellung dadurch geschaffen dass der kleine Pupillendurchmesser effektiv vergrossert wird Eine quantitative Abschatzung dieses Effektes wurde an anderer Stelle gegeben (2)

b) Von der Vergrosserung des nutzbaren Pupillendurchmessers abgesehen ist zu beachten das durch die Eindellung die betreffende Netzhautpartie nicht nur gegen das Rotationszentrum des Auges verschoben wird Eine Komponente der Eindellrichtung ist gegen die Pupille gerichtet wodurch der optische Weg des Beobachtungs und Beleuchtungsstrahles im Auge abnimmt Bei starker Turbiditat wird durch diese Verminderung der Schichtdicke und die damit ver

knüpfte Verminderung des Streulichtes im Beobachtungssystem die schlecht oder überhaupt nicht mehr sichtbare Retina oft wieder in deutliche Sehdistanz gerückt

3 Die optischen Auswirkungen der Aenderung des Auftreffwinkels des Beobachtungs und Beleuchtungsstrahles durch SI

Durch die Eindellung kommt es notwendigerweise zu einer Aenderung des Auftreffwinkels des Beobachtungs und Beleuchtungsstrahles hinsichtlich der beobachteten Netzhautregion wobei wir unter Auftreffwinkel den Winkel verstehen den der Beobachtungs- oder Beleuchtungsstrahl mit der in der Auftreffstelle an den Augapfel gelegten Tangente bildet Wir haben an einer anderen Stelle die Variation des Auftreffwinkels in Abhängigkeit vom Gesichtswinkel des einfallenden Strahlenbundels fur eine vorgegebene Eindelltiefe angegeben (2) Durch die Beobachtung unter schiefer Inzidenz werden die Strukturen perspektivisch verzerrt und machen eine Reihe von Formtransformationen durch Es ist eine einleuchtende Erfahrungstatsache dass die Erkennung und Identifikation pathologischer Stellen oft in einer ihrer Transformationsformen besonders leicht ist und die Struktur dann als besonders typisch erscheint Es ist ferner zu beachten dass die scheinbare Schichtdicke und damit die Transparenz der durchstrahlten semitransparenten Schichten vom Auftreffwinkel des Beobachtungsbundels abhangt Wie jedem Biomikroskopisten bekannt ist macht sich die durch den Beobachtungsstrahl senkrecht getroffene Netzhaut je nach dem beobachteten Netzhautareal als kaum wahrnehmbare (Peripherie) oder deutliche Verschleierung (Papillennahe) der darunter liegenden Chorioidea bemerkbar Bei kleinen Auftreffwinkeln des Beobachtungsbundels erscheint selbst in Ora serrata Nahe die Netzhaut opak Damit mussen aber auch die scheinbaren Kontraste der Strukturelemente die in der Netzhaut und Aderhaut eingelagers sind variieren

Die durch Variation des Auftreffwinkels des Beobachtungsstrahles erzeugten Veranderungen des Farbtones und der Sattigung eines betrachteten Netzhautareals werden aus dem Gesagten verstandlich

Die Aenderung der Differenz des Auftreffwinkels von Beleuchtungs und Beobachtungsbundel ist ein wichtiges diagnostisches Hilfsmittel da dadurch die Schichtdicke des optischen Schnittes kontrolliert wird Die letztere sollte nicht mit der erwahnten scheinbaren Schichtdicke verwechselt werden Die Schichtdicke des optischen Schnittes ist die in der Strahlrichtung gemessene Dicke des durch das Beleuchtungsbundel herausgeschnittenen durch Streulicht sichtbaren Gewebsschnittes

Es ist bekannt dass die Tiefenlokalisation und damit die raumliche Zuordnung zur Schicht in der ein Strukturelement liegt umso leichter ist je grosser die scheinbare Schichtdicke gewahlt wird Daraus folgt die Regel dass der

Winkel zwischen Beobachtungs und Beleuchtungsbundel so gross wie moglich gewahlt werden sollte

Optimale Beobachtungsbedingungen werden erfahrungsgemass in vielen Fallen durch die Inspektion eines Strukturelementes *im Profil erzielt* Durch Verschiebung des *Strukturelementes* auf die Hohe des Eindellungswalles wird das durch den Beleuchtungsstrahl getroffene Detail gegen einen entfernten defokussierten und damit dunklen und homogenen Hintergrund unter einem hohen scheinbaren Kontrast wahrgenommen.

Wie in III (1) und III (2) auseinandergesetzt *wurde* verbessern die bei der *Profilbetrachtung zur* Auswirkung kommende Vergrosserung des scheinbaren Kontrastes und die Vertauschung eines komplexen gegen einen homogenen Hintergrund die Sichtbarkeit eines schlecht erkennbaren Strukturelementes oft sehr stark Die Inspektion einer suspekten Netzhautregion bei verschiedenen Graden der Eindelltiefe *erweitert somit eindeutig unsere diagnostischen* Moglichkeiten

4 Die Bedeutung parallaktischer Bewegungen fur die Strukturerkennung

Es ist von grosser Wichtigkeit nicht nur statische Zustande wie wir sie in Kapitel IV *3 beschrieben haben zu betrachten sondern ein bestimmtes* kritisches Netzhautareal zu beobachten wahrenddem der Eindellungsdorn hin und her bewegt wird Eisner (8) hat unseres Wissens als erster auf den Wert dieser Untersuchungsmethode aufmerksam gemacht. Da der Unterschied im Parallaxwinkel zwischen Netzhaut und Chorioidea unter normalen Bedingungen zu gering ist wird hier bei Verschiebungen einer Fundusstelle durch den Eindellungsdorn meist keine parallaktische Bewegung der Schichten gegeneinander wahrgenommen

Unter pathologischen Bedingungen zum Beispiel beim Vergleich von geformten praeretinalen Corpustrubungen *mit retinalen Strukturen bei der* Gegenuberstellung von aufstehenden Lochrandern mit ahnlichen Strukturmustern der Retina und Chorioidea bewegen sich die in verschiedener Tiefe gelegenen Elemente und Verbande mit unterschiedlicher Winkelgeschwindigkeit, sobald eingedellt wird und konnen dadurch beleutend leichter voreinander unterschieden werden Es ist *gezeigt worden* (9) dass die Bewegungsperspektive nicht nur die Tiefenlokalisation einzelner Strukturelemente erleichtert oder uberhaupt erst ermoglicht vielmehr werden zerstreute Einzelelemente eines Strukturverbandes deren *Zusammengehorigkeit* zu erkennen unter statischen Bedingungen nicht moglich ist durch die Bewegungsperspektive zu einem einheitlichen Ganzen zusammengeschlossen Dieser Mechanismus wird von den Gestaltpsychologen als common fate bezeichnet Auf Grund dieses Phaenomens gelingt es oft die Zusammengehorigkeit schichtweise angeordneter regelloser und lockerer Strukturen und damit von Schichtgrenzen zu erkennen.

5 Die Verbesserung der Perzeption durch Kompression der Chorioidea

Die Chorioidea wirkt bekanntlich wie ein Rotfilter wobei sie durch das Beleuchtungsbundel zweimal durchlaufen wird Die genauesten Untersuchungen uber die spektraler Eigenschaften der Chorioidea scheinen von Geeraets et al *(10) zu stammen Es ist offensichtlich, dass das spektrale Verhalten der Chorioidea* nicht mit einer Blutschicht von aequivalenter Schichtdicke ubereinstimmt Man kann jedoch annehmen dass bei zunehmender Kompression der Chorioidalgefasse die Absorptionskurve der Chorioidea angenahert so verandert wird, als ob von der Gesamtabsorptionskurve der Chorioidea im gefullten Zustande die *Absorptionskurve einer Blutschicht von zunehmender* Schichtdicke subtrahiert wurde Prince (11) hat die Absorptionskurve fur Blutschichten variabler Dicke bekanntgegeben Die Chorioidea schneidet somit aus dem Emissionsband der Beleuchtungsquelle je nach Schichtdicke wichtige Anteile heraus und kann dadurch als Storfaktor wirken Bei der SI steigt durch Ausschaltung der Filterwirkung der Choriodea die Intensitat des von der Sklera ruckgestrahlten Lichtes und zwar vor allem im Grun und Blau fur welche das Sehorgan empfindlicher ist Damit wird das Pigment gegen einen helleren weissen Hintergrund unter verstarktem Kontrast wahrgenommen *An dieser Kontrast*steigerung ist indessen auch die Verbesserung der Abbildungsgute durch Reduktion des Gesichtswinkels in geringerem oder starkerem Masse beteiligt wie in (2) auseinandergesetzt wurde

Die Kontrasttransformation ist aber nicht vollstandig da einerseits wohl nie *eine vollige Kompression der Chorioidalgefasse gelingt* andererseits stets ein Anteil des eingestrahlten weissen Beleuchtungslichtes spektral unverandert zurückgestrahlt wird (12) Trotz dieser Restriktionen wirkt sich die Kontrastverstarkung und die Verbesserung der Sichtbarkeit wichtiger Strukturelemente in der Biomikroskopie klar und uberzeugend aus wie im Fall 1 gezeigt wird

Ohne Zweifel kann das chorioidale Rotlicht durch geeignete Sperrfilter (so genannte Rotfreifilter) im Beleuchtungs- oder Beobachtungsstrahlengang eliminiert werden die aber zwangslaufig ihrerseits wiederum spektrale Restriktionen einfuhren eine *Beobachtung des Fundus im polychromatischen* Licht unmoglich machen und damit zu einem Informationsverlust fuhren Wir haben wiederholt beobachtet dass die Kompression der Chorioidea wirkungsvoller ist als jede Manipulation mit spektral selektiven Filtern um bestimmte Strukturelemente der Retina und Chorioidea zur Darstellung zu bringen

6 Die Auswirkung besonderer Untersuchungsbedingungen auf die Perzeption in der Biomikroskopie

Wir schildern in folgenden einige Effekte deren Erklarung umstritten ist und die auch noch andere Deutungsmoglichkeiten zulassen

Es geht uns in erster Linie darum anzuregen dass alle apparativen Moglich

keiten ausgeschopft werden Es ist oft auffallend dass die Erkennbarkeit von Struktureinzelheiten *von deren* Orientierung abhangt d h ob sie wagrecht schrag oder senkrecht im Bildfeld erscheinen Dies setzt naturlich voraus dass die beobachtete Struktur eine oder mehrere Symmetrieachsen besitzt Takala (13) hat gezeigt dass die Komponenten komplexer Figuren *die eine vertikale* Symmetrieachse besitzen besser erkannt werden Fitts et al (14) gelangten zum selben Schluss Ein einfaches Mittel um die Orientierung beobachteter Strukturen zu andern das aber nur eine begrenzte Wirkung hat besteht in der Rotation des Spiegels des Goldmannglases Da die Spiegel ausreichend gross sind kann in vielen Fallen das Kontaktglas betrachtlich gedreht und damit die Orientierung der beobachteten Struktur geandert werden bis das beobachtete Netzhautareal aus dem Gesichtsfeld hinauswandert

Die relative *Orientierung der Grenzen des ausgeleuchteten Beobachtungs*feldes oder Beobachtungsspaltes zu der beobachteten Struktur ist nicht irrelevant Auch hier muss offensichtlich das Vorhandensein einer oder mehrerer Symmetrieachsen gefordert werden damit das Phaenomen zur Beobachtung kommt

Je nach Ausrichtung der Struktur zu den Grenzen des uberlagerten Lichtspaltes oder des Lichtstreifens kann diese besser oder weniger gut erkannt werden Kopfermann (15) hat auf diese Zusammenhange aufmerksam gemacht und sie naher untersucht Wir haben es in der Hand den Spalt oder den Lichtstreifen je nach der Strukturorientierung auszurichten und zu prufen ob in dem betrachteten Falle eine Verbesserung der Erkennbarkeit eintritt oder nicht.

Wir sind Adelheid Meyer fur die Ausfuhrung der Funduszeichnungen zu grossem Dank verpflichtet

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From the Department of Ophthalmology University of Umea and University of Uppsala and the Department of Pharmacology University of Uppsala Sweden

EFFECT OF A MERCURIAL DIURETIC MERSALYL ON IN VITRO SECRETORY ACTIVITY OF THE RABBIT EYE CILIARY PROCESSES

BY

LENNART BERGGREN

Organic mercurials are diuretics *in vivo* They inhibit tubular reabsorption of sodium and chloride Compounds marketed for injection as Mersalyl® contain the organic mercury compound mersalyl and equimolar amounts of theophyl line in order to promote absorption and decrease of local irritation upon intra muscular injection These amounts of theophylline do not themselves exert diuretic effect

In vivo and *in vitro* mercury inhibits cation transport in the kidney (9) It prevents the active uptake of sodium and potassium from the medium in the Crustacaean Daphnia Magna (14) and inhibits the sodium transport in the frog skin (17)

Dimercaprol BAL is a dithiol and the capacity to complex with mercury is often strong enough to abolish the effect of mercurial diuretics

The action of mercury on active cation transport made it of interest to inve stigate if the drug could influence *in vitro* secretory activity of the ciliary pro cesses of the eye

Material and Methods

Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used

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Secretory pumping *in vitro* has been described in detail previously (3 4) The gradual shrinkage in size that the ciliary processes show on incubation in a physiologic buffer solution was taken as a measure of secretory activity The tissue fluid of the ciliary processes was replaced with a physiologic buffer solution by perfusion through a carotid artery in the living animal Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution Care was taken to prevent secretion as much as possible up to the incubation *in vitro* The area of a transverse optical section of the process s was photographed intermittently for one hour and one to four processes were generally suitable for planimetry The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time. The single eye was treated as the statistical unit Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function Those with a shrinkage of 15 per cent or more at 5 minutes were assumed to have too small a residual capacity In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes Blocking effects on secretion were considered to have occurred if the curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line This criterion allows relatively small samples to be used

Mersalyl injections in vivo In order to investigate if mersalyl injected *in vivo* might have any effect on secretory pumping of the ciliary processes *in vitro* without mersalyl in the bathing medium the following experiments were performed Six rabbits were given 1 ml of mersalyl intramuscularly on two consecutive days *In vitro* experiments of secretory pumping were done on three rabbits one hour after the last injection and on three rabbits one day after the last injection Because no drug is added to the bathing medium a slightly different standard curve is used as described previously (4)

Drugs

Buffer solution The physiological buffer solution was made up as described previously (4) and prepared from chemicals of analytical grade With the concentrations expressed in mM/L the composition was NaCl 150 KCL 3 $MgSO_4$ 7 H_2O 1 glucose [illegible] The solution was tris buffered and equilibrated with 95 per cent O_2/5 per cent CO_2 to a pH of 7 4

Mersalyl Mersalyl® (ACO Sweden) Ampoules of 2 ml containing 100 mg mersalyl and 50 mg theophylline per ml Mersalyl mol w 506 Theophylline mol w 180

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Dimercaprol BAL (Boots Pure Drug Co Ltd England) Only injection of dimerca

prol 0 05 g dimercaprol/ml of arachis oil containing 10 % benzyl bensoate Ampoules of 2 ml Dime caprol mol w 124

Results

Mersalyl in the bathing medium Mersalyl caused a pronounced effect on secretory pumping In the final part of the experiment the area of the ciliary processes increased when a concentration of mersalyl from 0 1 mg/ml was used A concentration of 0 2 mg/ml (4 × 10^{-4} M) resulted in an increase at 60 min up to 116 per cent of the zero time value A concentration of 0 01 mg/ml was without effect (Fig 1)

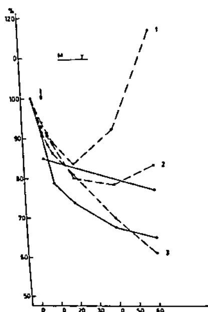


Fig 1

Mersalyl added to the bathing solution at arrow Ordinate = calculat on of transverse sect on area of ciliary processes in per cent Zero value = 100 per cent Abscissa = t me in minutes Mean selected time shrinkage curves Curve 1 = 0 2 mg/ml mersalyl 4 × 10^{-4} M (5 an mals 12 processes) Curve 2 = 0 1 mg ml mersalyl (5 animals 7 pr cesses) Curve 3 = 0 01 mg ml mersalyl (5 an mals 11 processes) Continuous curve mean s lected standard curve with buffer solution, pH 7 4 Minimum slope line from 85 per nt at 5 minutes to mean standard value plus three standard deviations at 60 minutes

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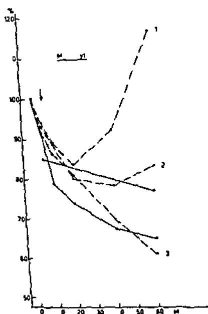


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Mersalyl® solution contains theophylline The final concentration in the bathing medium was 0 1 mg/ml of theophylline when the highest concentration of mersalyl (= 0 2 mg/ml) was used Experiments with theophylline only, using a tenfold concentration i e 1 0 mg/ml, was without effect on the normal shrinkage of the ciliary processes (Fig 2)

Dimercaprol BAL was without effect on the normal shrinkage of the ciliary processes in a final concentration of 4×10^{-4} M The effect of mersalyl could be blocked by an equimolar concentration of BAL (BAL 4×10^{-4} M and mersalyl 4×10^{-4} M) (Fig 2)

Mersalyl injections in vivo After mersalyl injections *in vivo* the succeeding *in vitro* experiments without any drug in the bathing medium did not show any effect on secretory pumping differing from normal conditions The two groups were similar The first group had a mean value at 60 min of 55 6 per cent (3 animals 9 processes) and the second group a mean value at 60 min of 53 2 per cent (3 animals 7 processes) The combined group is recorded in fig 3

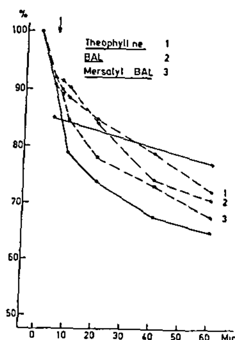


Fig 2

Theophylline dimercaprol BAL and theophylline plus dimercaprol BAL added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Curve 1 = Theophylline 1 mg/ml (6 animals 13 processes) Curve 2 = BAL 4×10^{-4} M (3 animals 5 processes) Curve 3 = Mersalyl 4×10^{-4} M plus BAL 4×10^{-4} (4 animals 11 processes) Mean selected standard curve and minimum slope line as in fig 1

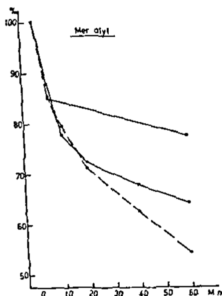


Fig 3

Mersalyl 2 × 1 ml injected intramuscularly *in vivo* Coordinates as in fig 1 Discontinuous curve (6 animals 16 processes) *Continuous curve = mean standard curve with* buffer solution, pH 7 4 Minimum slope line from 85 per cent at 5 minutes to mean value plus three standard deviations at 60 minutes

Since in these experiments the drug is added before the *in vitro* experiment a slightly different standard curve is used (4)

Discussion

The *formal nature of the mechanism of* organic mercurials on transport is complex and not yet wholly elucidated The action of mercurials in the kidney might partly be explained by changes in permeability of cellular membranes but primarily it involves an attachment of mercury to a sulfhydryl group of an enzyme that helps to generate energy for sodium transport or to a sodium carrier

Swelling of rat kidney slices have been observed after treatment with orga

nic mercurials (16 19) It was suggested that this effect was due to an increased cell permeability rather than to an effect on active transport

Bivalent mercury has a great affinity for sulfhydryl groups of protein molecules It has been assumed that the mercuric ion of organomercurial diuretics inhibits the enzymes involved in sodium transport by forming a mercaptide complex with the enzyme protein Mercury which reacts with sulfhydryl groups of tissues may be removed from the receptor sites by the sulfhydryl compound dimercaprol, BAL A reduction of proteinbound sulfhydryl groups is correlated with the occurrence of diuresis The diuretic effect of mercurials is apparently not due to inhibition of succinic dehydrogenase since therapeutic doses of mersalyl fail to inhibit oxidative enzymes of the Krebs cycle Inhibition of succinate dehydrogenase in the kidney tubules with organic mercurials occurs only after heavy doses

It can be noted however that in the ciliary processes in the eye there is histochemical evidence for succinic dehydrogenase (2 10 12) Furthermore, Cole (13) could establish in *in vitro* experiments that succinate and citrate increased the transepithelial potential and the short circuit current of the ciliary processes Cole suggested that the active sodium transport from stroma to aqueous is driven from the citric acid cycle oxidation

A considerable body of experimental evidence now suggests that the Na K dependent ATPase activity found in different epithelial cell membranes (7 18 21) including the ciliary processes of the eye (6 20) is a property of the coupled transport for sodium and potassium in the membrane Recently Jones et al (15) established that organic mercurials *in vitro* and *in vivo* inhibited Na K dependent ATPase activity in membrane fragments from kidneys of rats It was suggested that the mercurials act by directly attacking sodium and potassium binding sites of the transport system (see also review by Cafruny (9) 1968)

As well as in the kidney mersalyl inhibits active transport in other epithelial systems as for instance in the frog skin Using about the same concentration as in our experiments Linderholm (17) found that mersalyl (10^{-4} M) inhibited active transport of sodium across the frog skin *in vitro*

With the present *in vitro* technique the influence on transport by various drugs can be studied The direction of the transport is more difficult to analyze. The net result of a less than normal shrinkage of the ciliary processes would indicate an inhibited secretion of aqueous This effect could be due to a decreased transport "inwards" to the aqueous side or to a stimulated transport "outwards" to the ciliary stroma A toxic effect leading to a complete stoppage of transport by cell death would with similar outer and inner environment of the processes be expected to lead to a preservation of the zero time value of the area of the ciliary processes An enlargement instead of a shrinkage of the processes (i e a swelling of the stroma) would indicate a stimulated transport "outwards" to the ciliary stroma with accompanying water It is then

assumed that the technique is an indicator of a transport across the membrane system (i e *from outside to inside*) The photographic recordings which in previous experiments (3 4,5) showed a uniform decrease in area with time lent support to this view

An enlargement of the ciliary processes as was found in the present experiments is compatible with a swelling of the stroma but on the other hand a swelling in the epithelial cells cannot be *ruled out* *It is not possible from* the present data to decide conclusively between these alternatives A suggestion that a stromal process is here also involved is the fact that the pictures from *experiments with strong mersalyl* concentrations showed ciliary processes which increased uniformly exactly as in previous experiments there was a uniform decrease It would be difficult to understand that if there had been a swelling in the epithelial cells this would occur to the same extent over the whole area resulting in a uniform increase An irregular increase of the ciliary processes *would seem more likely if the swelling had occurred in the epithelial cells*

With the technique used mercury is as yet the only drug found to have caused an enlargement instead of a shrinkage of the ciliary processes Pilocarpine epinephrine acetazoleamide and metabolic inhibitors as for instance ouabain all gave a less than normal shrinkage (3 4 5)

If organic mercury should exert a similar action in the ciliary processes as in other epithelial transport systems the observed enlargement of the ciliary processes after mercurial treatment might be compatible with different possibilities

An increased membrane permeability might be expected to lead to a swelling in the epithelial cells but in the absence of an osmotic gradient it would not lead to a swelling of the stroma An inhibition of the sodium pump in the ciliary epithelial membrane system would cause a swelling in the epithelial cells An effect *on coupled opposing systems of transport of ions and water* across the ciliary epithelial cell layers would hypothetically result in a swelling of the stroma These transport systems are then asumed to work with some kind of feedback system in such a manner that an inhibition of for instance a transport system inwards (i e the sodium pump) would lead to the stimulation of another process of transport of *ions and water in the opposite direction*

The negative results on the secretory activity in the eye from animals injected with mersalyl *in vivo* were not unexpected The organic mercurials have been shown to have a selective affinity to the kidney (8) and such diuretics did not produce a fall in intraocular pressure in human subjects (11) The reported transitory decrease in IOP in normal and nephrectomised rabbits from intramuscular injections of organic mercurials *in vivo* (1) can hardly be taken as evidence for a block of the sodium pump in the ciliary epithelium. The authors were also unable to demonstrate any effect from subconjunctival or topical administration

Summary

Mersalyl in a concentration from 0 1 mg/ml in the bathing medium caused an enlargement of the rabbit ciliary processes *in vitro* Theophylline was without effect. Dimercaprol BAL which in itself was without effect on the secretory pumping of the ciliary processes abolished in equimolar concentration the mersalyl effect *In vivo* injections of mersalyl were without effect Influence on secretion *in vitro* and particularly across the ciliary epithelial cell membranes is difficult to interpret in terms of directions of transport The action of mersalyl on the ciliary processes *in vitro* is discussed in relation to its presupposed action on other epithelial active transport systems It is suggested that the marked effect of mersalyl causing an enlargement instead of the normal shrinkage of the ciliary processes with time might be due to interference with active cation transport possibly by its action on Na K dependent ATPase or on enzymes of the citric acid cycle Blocking of transport to the aqueous side or stimulation of transport to the stroma are both potential possibilities

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SECRETORY ACTIVITY IN VITRO OF THE RABBIT EYE CILIARY PROCESSES INCUBATED WITH CORTICOSTEROIDS NEUROHYPOPHYSEAL HORMONES AND ASCORBIC ACID

BY

LENNART BERGGREN

Corticosteroids have pronounced effects on the exchange of sodium and potassium but a full analysis of their effects on transport mechanisms and directions of transport is still lacking The mineral corticoids stimulate the sodium hydrogen (or potassium) exchange in the distal tubules and they decrease the sodium content and increase the potassium content in for instance sweat and saliva In the eye corticosteroids have well established pressure increasing effects on intraocular pressure Here also their basic action is unsolved although the pressure increasing effects are mostly attributed to effects on outflow facility Possible effects on secretion however have never been ruled out Linner (22 23) has presented evidence that prednisolone caused an elevation of the intraocular pressure with no change in the facility of outflow or in the episcleral venous pressure The effect was explained to be caused by an increase in the rate of aqueous flow It can be noted that Jackson & Waitzman (20) reported a dual intraocular pressure response and the secondary hypertensive response was accompanied by changes in flow They could also demonstrate a sustained hypotension by aldosterone probably caused by decreased aqueous flow

However aldosterone has a stimulatory effect on sodium transport in *in vitro* experiments on toad bladder (12) and Cole (10) showed that the aldosterone antagonist spirolactone reduced sodium and water influx across the ciliary epithelium in the rabbit eye

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The vasopressor hormone of the posterior pituitary lobe has well known effects on the resorption of water by its action on the renal tubules Becker et al (3 11) have tested vasopressin on human and rabbit eyes Vasopressin lowered the intraocular pressure when applied locally and tonography revealed that the intraocular pressure drop was due to suppression of aqueous flow

Neurohypophyseal hormones increase *in vitro* the rate of water uptake and the rate of active sodium transport across the frog skin (15) and the toad bladder (14) presumably by increasing the pore size of some layer in the skin

Ascorbic acid is secreted into the aqueous humor in excessive amounts but its action on the inflow and/or outflow is not clearly understood A review of the possible functions of ascorbic acid in the eye is given by Heath (18) In normal human subjects Linner (24 25) could show that oral and topical administration of ascorbic acid gave a small but significant decrease of the intraocular pressure Oral dosages of 0 5 1 0 g/day or application of a 10 per cent eye drop solution three times a day were given in order to influence the intraocular pressure The experimental results were in favour of a reduction in the rate of flow The findings have been confirmed (9) but failures to decrease IOP with ascorbic acid are also reported (13 17)

In the present paper the previously described method of studying secretory activity of the ciliary processes *in vitro* was used (6 7) in order to determine if corticosteroids neurohypophyseal hormones or ascorbic acid could influence this type of secretory activity

Material and Methods

Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used

In vitro technique Secretory pumping has been described in detail previously (6) The gradual shrinkage in size that the ciliary processes show on incubation in a physiologic buffer solution was taken as a measure of secretory activity The tissue fluid of the ciliary processes was replaced with a physiological buffer solution by perfusion through a carotid artery in the living animal Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution Care was taken to prevent secretion as much as possible up to the incubation *in vitro* The area of a transverse optical section of the processes was photographed intermittently for one hour and one to four processes were generally suitable for planimetry The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time The single eye was treated as the statistical unit Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function Those with a shrinkage of 15 per cent or more at 5 minutes

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Table 1

Shrinkage of ciliary processes *in vitro* after incubation with various drugs. Effect 0 = normal *shrinkage*. Buffer solution pH 7.4 unless otherwise indicated

Drug	Number of expts animals/processes	Final conc/ml in medium	Effect
Hydrocortisone	4/9	1 mg	0
Prednisolone	4/8	0.5 mg	0
Dexamethasone	4/11	0.05 mg	0
Dexamethasone i.m.[1]	7/21		0
Aldosterone	4/11	0.01 mg	0
Corticotropin	6/12	0.01 IU	0
Corticotropin i.m.[2]	6/17		0
Vasopressin	4/10	0.2 IU	0
Oxytocin	5/14	0.1 IU	0
Ascorbic acid	3/16	20 μg	0
Ascorbic acid	3/12	100 μg	0
Ascorbic acid[3]	5/20	100 μg	0
Ascorbic acid	2/8	200 μg	0
Ascorbic acid	8/15	1 mg	0
Ascorbic acid[4]	6/13	1 mg	0
Ascorbic acid pH 7.0[4]	5/13	1 mg	0

1) 4 mg dexamethasone i.m. during 3 days before *in vitro* experiment
2) 15 IU corticotropin 6 and 3 days before *in vitro* experiment
3) Ascorbic acid added to the perfusion fluid as well as to the bathing solution in a concentration of 100 microg/ml
4) Ascorbic acid added to the bathing solution 6 times during the first half hour of the *in vitro* experiment

were below a line from 85 per cent at 5 minutes to the mean value plus 3 standard deviations at 60 minutes. Table 1 and fig. 1.

Ascorbic acid. The effect of ascorbic acid was tested in various ways. The results are based from a total of 32 rabbits. Table 1.

With the common *in vitro* technique ascorbic acid was put into the bath at plus 5 minutes. A concentration from 20 microg/ml to 1 mg/ml final concentration in the bathing medium was without effect on the normal shrinkage of the ciliary processes.

The effect of ascorbic acid was also tested with ascorbic acid in a concentration of 100 microg/ml in the perfusion fluid as well as in the bathing medium and a pH 7.4. These results also were negative.

In order to eliminate a possible oxidation of ascorbic acid during the *in vitro*

were assumed to have too small a residual capacity In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes Blocking effects on secretion were considered to have occurred if the mean curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line This criterion allows relatively small samples to be used Detail variations of the technique is reported under Results

Drugs

Buffer solution The physiological buffer solution was made up as described previously (7) and prepared from chemicals of analytical grade With the concentrations expressed in mM/L the composition was NaCl 150 KCL 3 Mg SO_4 7 H_2O 1 glucose 7 The solution was tris buffered and equilibrated with 95 per cent O_2/5 per cent CO_2 to a pH of 7 4 or in some experiments 7 0

Hydrocortisone Solu Cortef® hydrocortisone sodium succinate 50 mg/ml Ampoules of 2 ml (Upjohn Co Mich U S A)

Prednisolone Precortalon aquosum® prednisolone sodium succinate 25 mg/ml Ampoules of 1 ml (Organon Holland)

Dexamethasone Decadron® fluor methyl prednisolone 4 mg/ml Ampoules of 1 ml (M S D U S A)

Aldosterone Aldocorten® 0 5 mg/ml Ampoules of 1 ml (Ciba Switzerland)

Corticotropin Cortrophine® 10 IU/ml Ampoules of 5 ml (Organon Holland)

Vasopressin Postacton® 20 IU/ml Ampoules of 1 ml (Ferring Sweden)

Oxytocin Partocon® 10 IU/ml Ampoules of 1 ml (Ferring Sweden)

Ascorbic acid 500 mg/ml Ampoules of 1 ml (ACO Sweden)

Results

Corticosteroids and neurohypophyseal hormones The results from 44 rabbit experiments are summarized in table I

It was not possible to influence significantly the *in vitro* secretory activity by the administration in the bathing medium of the following drugs Hydrocortisone prednisolone dexamethasone (fig 1) aldosterone corticotropin vasopressin and oxytocin The effect of dexamethasone and corticotropin was also tested after intramuscular injection of these drugs Dexamethasone (4 mg) was given during 3 days before the *in vitro* experiment Corticotropin (15 IU) was given 6 and 3 days before the *in vitro* experiment The *in vitro* secretory activity was then studied without addition of any drug in the bathing medium The results from these experiments were also within normal limits

The mean curves from all these experiments showed a gradual shrinkage of the ciliary processes which was within the defined normal range i e the curves

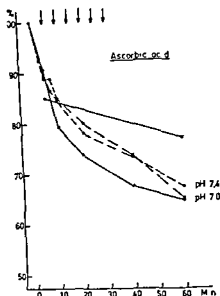


Fig 2

Ascorbic acid added to the bathing solution at arrows (final concentration in the bath 1 mg ml) Coordinates as in fig 1 Mean selected time shrinkage curves Curve pH 7 4 (*4 animals 13 processes*) Curve pH 7 0 (5 animals 13 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

ciliary *processes* and ultimately on aqueous secretion With regard to the effects on sodium and potassium transport in other epithelial systems by corticosteroids a similar effect in the ciliary processes would not have seemed unlikely On the other hand the negative results cannot be taken as evidence that corticosteroids do not influence transport in the ciliary processes of the eye It can be noted that corticosteroids have structural similarities to the cardiac aglucones like ouabain This drug has repeatedly been shown to have a strong inhibitory effect on active sodium transport in many epithelial systems including the eye (4 7 9) The strong effect of ouabain and the weak effect of corticosteroids on cation *transport over the erythrocyte membrane has led to the hypothesis* advanced by Glynn (16) that corticosteroids in order to be effective have to be transformed to substances similar to the cardiac aglucones Since a transformation of this kind is unlikely to occur *in vitro* possible effects will not easily be demonstrated

The stimulating effect of the neurohypophyseal hormones and aldosterone on the transport of sodium ions across amphibian epithelial layers *in vitro* has been established for frog skin (15) as well as for toad bladder (12 14) The results are in support of the idea of a permeability effect Spirolactone an aldo

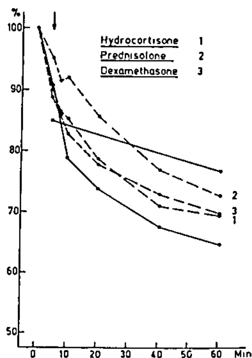


Fig 1

Hydrocortisone prednisolone and dexamethasone added to the bathing solution at arrow Ordinate = Calculation of transverse section area of ciliary processes in per cent Zero value = 100 per cent Abscissa = time in minutes Mean selected time shrinkage curves Curve 1 = Hydrocortisone succinate 1 mg/ml (4 animals 9 processes) Curve 2 = Prednisolone succinate 0 5 mg/ml (4 animals 8 processes) Curve 3 = Dexamethasone 0 05 mg/ml (4 animals 11 processes) Continuous curve = mean selected standard curve with buffer solution pH 7 4 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

experiment the following change was made in the *in vitro* technique Of the total dose giving a final concentration of 1 mg/ml in the bath 50 per cent of the drug was given at plus 5 minutes and 10 per cent of the drug then every 5 minutes up to 30 minutes incubation time Two pH values pH 7 4 and pH 7 0 were tested with this technique Both series were within normal limits

Summing up ascorbic acid was without effect on the normal secretory activity *in vitro* of the ciliary processes of the rabbit eye at pH 7 4 and 7 0 and it was also ineffective if administered to the bathing medium intermittently during half an hour or if the bathing medium as well as the perfusion fluid contained ascorbic acid

Discussion

The present *in vitro* experiments could not establish any potential role of corticosteroids or of neurohypophyseal hormones on transport processes in the

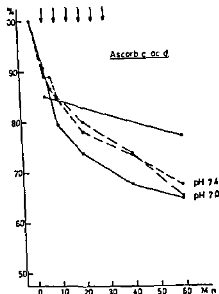


Fig 2

Ascorbic acid added to the bathing solution at arrows (final concentration in the bath 1 mg/ml) Coordinates as in fig 1 Mean selected time shrinkage curves Curve pH 7 4 (6 animals 13 processes) Curve pH 7 0 (5 animals 13 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

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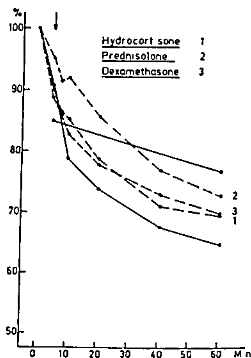


Fig 1

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Discussion

The present *in vitro* experiments could not establish any potential role of corticosteroids or of neurohypophyseal hormones on transport processes in the

sults are in support of the idea of a permeability effect Spirolactone an aldo on *in vitro* secretion by ascorbic acid indirectly support this latter view

The same kind of reasoning could be *adopted towards* some effects of corticosteroids The absence of effect by corticosteroids on *in vitro* secretory pumping (in the present experiments) and on aqueous flow (1) (measured by fluorophotometry) favour a hypothesis that the pressure increase found by Linner (2? 23) without change in C values (measured by tonography) or in F values (measured by the suction cup) might be due to an effect on routes of outflow via unconventional routes

Summary

The shrinkage of ciliary processes *in vitro* is taken as a measure of secretory activity It was not posible to influence the normal shrinkage with time with the following drugs and concentrations in the bathing medium Hydrocortisone 1 mg/ml prednisolone 0 5 mg/ml dexamethasone 0 05 mg/ml aldosterone 0 01 mg/ml corticotropine 0 01 IU/ml vasopressin 0 2 IU/ml oxytocin 0 1 IU/ml and ascorbic acid up to a concentration of 1 mg/ml

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sterone antagonist reduced sodium and water influx across the ciliary epithelium in the rabbit eye (10)

In the present *in vitro* experiments there was no effect from neurohypophyseal hormones or aldosterone It should be noted however that the present *in vitro* technique is more appropriate to demonstrate inhibition than stimulation A hypothetical stimulation would give rise to an increased rate of shrinkage or a more pronounced total shrinkage at the end of the experiment This would be difficult to show since the normal shrinkage curve has already a rather steep slope and the 60 minutes value is probably a lower limit value Further incubation does not cause a further shrinkage of the ciliary processes

The excess of ascorbic acid in the aqueous and its selective transport mechanism has for a long time been a subject of considerable research work but there is still surprisingly little knowledge of its basic role in the eye (see reviews by Kinsey (21) and Linnér (26)) Among pertinent questions which still remain to be answered are a) how ascorbic acid itself is transported into the aqueous b) whether ascorbic acid might be a necessary component in other active transport processes across the ciliary epithelial layers c) or whether the excess of ascorbic acid in the aqueous might play a role in metabolic processes in the anterior parts of the eye for instance on the outflow resistance in the trabecular meshwork

Ascorbic acid is transported into the retina as well as into the aqueous via the ciliary processes In the retina the transport is linked with the movement of sodium and the transport is inhibited by ouabain and DNP (19) In the ciliary processes the active sodium transport and the secretory pumping with our technique show similar characteristics (see review by Linner (26)) Furthermore Becker (5) has demonstrated that the accumulation of ascorbic acid in ciliary body preparations from guinea pigs was inhibited by ouabain and DNP The accumulation was also dependent on the presence of Na and K These findings suggested that the ascorbic acid transport in the ciliary processes was closely related to Na K dependent ATPase activity

The findings by Linner (24 25) that ascorbic acid *in vivo* could produce a fall in IOP gave rise to the present *in vitro* experiments However with our technique an excess of ascorbic acid did not influence the normal secretory activity in the ciliary processes Unfortunately there is no way of demonstrating the possible effects of the reversed condition i e a total lack of ascorbic acid Even animals on the point of death from scurvy (scurbutic guinea pigs) have apparently sufficient content of ascorbic acid in the aqueous (27)

Since the pressure drop by ascorbic acid in Linnér s (24 25) *in vivo* experiments occurred without change in C values it seemed likely that it was caused by a decrease in flow However Linner also discussed the hypothetical possibility that in his experiments an effect on outflow via unconventional uveoscleral routes as described by Bill (8) might be involved Our negative results

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FURTHER STUDIES ON THE EFFECT OF AUTONOMOUS DRUGS ON IN VITRO SECRETORY ACTIVITY OF THE RABBIT EYE CILIARY PROCESSES

A Inhibition of the pilocarpine effect by isopilocarpine arecoline and atropine
B Influence of isoproterenol and norepinephrine

BY

LENNART BERGGREN

The blocking effect of pilocarpine on the secretory pumping *in vitro* of the rabbit eye ciliary processes has been established repeatedly (5 6) In the present experiments the pilocarpine concentration in the bathing medium was 10 M final concentration which was regarded as giving a reliable blocking effect.

Another parasympatomimetic alkaloid arecoline had no significant effect up to a concentration of 10^{-5} M in previous experiments (5) The parasympatolythic agent atropine inhibited secretory activity *in vitro* only in a concentration of 10^{-5} M but not at 10^{-7} M (5)

The experimental set up does not allow different drugs to be added successively to the medium in the same experiment The period for studying drug effects is restricted to between 5 60 minutes A time of up to 5 min is needed to check that the surviving ciliary processes are in normal condition and after one hour the ciliary processes have pumped themselves dry and might be regarded as less viable Thus in order to study drug interaction each drug must be tested separately as well as simultaneously

The demonstrated inhibitory effect of epinephrine on the normal shrinkage

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The solution was tris buffered and equilibrated with 95 per cent O_2/5 per cent CO_2 to a pH of 7 4 or in some experiments 7 0

Pilocarpine Mol w 208 The hydrochloride was used

Atropine Mol w 289 The sulfate was used

Isopilocarpine Mol w 208 The stereoisomer of pilocarpine The hydrochloride was used The supply of isopilocarpine was a generous gift from Dr H W Voigtlander E Merck AG Darmstadt Germany

Arecoline Mol w 155 The hydrobromide was used

Isoproterenol Mol w 211 Isoproprydin® isoproterenolsulfate (Abbot Lab Chicago Ill U S A) 10 per cent dry powder ampoule

Norepinephrine Mol w 169 Nor Exadrin Conc® norepinephrine 1 base (Astra Sodertalje Sweden) Ampoules of 2 ml containing 1 mg norepinephrine base/ml

Results

Pilocarpine in a final concentration of 10^{-5} M once more had a blocking effect on the shrinkage of the ciliary processes *in vitro* (5 animals 19 processes) (Fig 1)

Atropine in a final concentration of 10^{-7} M was without effect (6 animals 17 processes) (Fig 1) In previous experiments (5) a possible inhibition at 10^{-7} M was noted Rabbits are in general rather insensitive to atropine compared to humans and monkeys but the sensitivity can differ in different strains of rabbits

A combination of pilocarpine 10^{-5} M and atropine 10^{-7} M was without effect on the normal shrinkage of the ciliary processes (6 animals 17 processes) In fact the pilocarpine atropine curve was very similar to the normal curve (Fig 1)

Pilocarpine atropine experiments were also done with a more uniform animal group in the following manner The *in vitro* experiments were repeated with one pilocarpine experiment one atropine experiment and one pilocarpine atropine experiment each day for three days and in a variable order The experiments on the same day were performed on animals from the same stock The results above were confirmed Pilocarpine 10^{-5} M (3 animals 11 processes) gave an inhibition Atropine 10^{-7} M (3 animals 10 processes) gave no inhibition The combination pilocarpine 10^{-5} M and atropine 10^{-7} M (3 animals 7 processes) gave no inhibition (Fig 2) These experiments showed that it is possible to abolish the pilocarpine effect on secretion *in vitro* by atropine

The stereoisomer of pilocarpine isopilocarpine gave a gradual inhibition of the shrinkage of the ciliary processes but even at a final concentration of 10^{-4} M it did not fulfill the given criteria for a blocking effect on secretion (Fig 3) It was thus not possible to reproduce the pilocarpine effect using its stereoisomer isopilocarpine Furthermore a combination of isopilocarpine

of the ciliary processes (5) made it of interest to test also other adrenergics such as the alpha adrenergic norepinehrine and the beta adrenergic isopro terenol

Material and Methods

Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used

In vitro technique Secretory pumping has been described in detail previously (3 4) The gradual shrinkage in size that the ciliary processes show on incubation in a physiological buffer solution was taken as a measure of secretory activity The tissue fluid of the ciliary processes was replaced with a physiological buffer solution by perfusion through a carotid artery in the living animal Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution Care was taken to prevent secretion as much as possible up to the incubation *in vitro* The area of a transverse optical section of the processes was photographed intermittently for one hour and one to four processes were generally suitable for planimetry The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time The single eye was treated as the statistical unit Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function Those with a shrinkage of 15 per cent or more at 5 minutes were assumed to have too small a residual capacity In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes Blocking effects on secretion were considered to have occurred if the mean curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line This criterion allows relatively small samples to be used

In vivo In some experiments drugs were injected *in vivo* prior to the perfusion In these experiments the *in vitro* incubation was done with buffer solution only and without the addition of test drugs A slightly different standard curve is then used as described previously (4)

Drugs

Buffer solution The physiological buffer solution was made up as described previously (4) and prepared from chemicals of analytical grade With the concentrations expressed in mM/L the composition was NaCL 150 KCL 3 $MgSO_4$ 7 H_2O 1 glucose 7

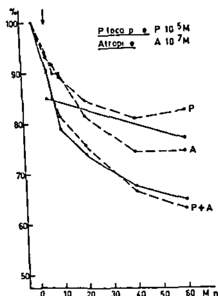


Fig 9

Pilocarpine, atropine and pilocarpine plus atropine added to the bathing solution at arrow. Coordinates as in fig. 1. Mean selected time shrinkage curves. Animals from the same stock and one experiment of each kind on the same day. Curve P = pilocarpine 10^{-5} M (3 animals, 11 processes). Curve A = atropine 10^{-7} M (3 animals, 10 processes). Curve P + A = pilocarpine 10^{-5} M plus atropine 10^{-7} M (3 animals, 7 processes). Continuous curve = mean selected standard curve and minimum slope line as in fig. 1.

perfusion was without effect on the normal shrinkage of the ciliary processes (Fig. 6). Pilocarpine but not isopilocarpine caused immediately a profuse salivation.

Isoproterenol sulfate in a final concentration of 0.2 mg/ml in the bathing medium (6×10^{-4} M) did not affect the normal shrinkage of the ciliary processes at a pH of 7.0 (6 animals, 15 processes) (Fig. 7).

Norepinephrine up to a final concentration of 0.01 mg/ml in the bathing medium (6×10^{-5} M) did not affect the normal shrinkage of the ciliary processes at a pH of 7.0 (6 animals, 12 processes) (Fig. 7).

Discussion

In previous experiments pilocarpine caused a less than normal gradual shrinkage of the ciliary processes *in vitro* (5, 6). The findings were interpreted as an

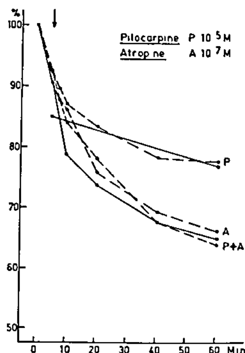


Fig 1

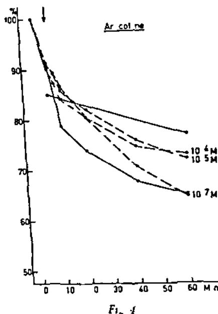
Pilocarpine atropine and pilocarpine plus atropine added to the bathing solution at arrow Ordinate = calculation of transverse section area of ciliary processes in per cent Zero value = 100 per cent Abscissa = time in minutes Mean selected time shrinkage curves Curve P = pilocarpine 10^{-5} M (5 animals 19 processes) Curve A = atropine 10^{-7} M (6 animals 17 processes) Curve P + A = pilocarpine 10^{-5} M plus atropine 10^{-7} M (6 animals 17 processes) Continuous curve = mean selected standard curve with buffer solution pH 7 4 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

10^{-5} M and pilocarpine 10^{-5} M was without effect on the normal shrinkage of the ciliary processes (Fig 5)

Experiments with arecoline in a final concentration of 10^{-7} M to 10^{-4} M in the bathing medium suggest an effect but even the results from 10^{-4} M experiments were within normal limits (Fig 4) This confirms previous data (3) The pilocarpine effect was abolished by a combination of arecoline 10^{-5} M and pilocarpine 10^{-5} M (5 animals 23 processes fig 5) as well as by arecoline 10^{-7} M and pilocarpine 10^{-5} M (6 animals 14 processes)

A combination of the ineffective concentrations of isopilocarpine 10^{-5} M and arecoline 10^{-5} M (7 animals 24 processes fig 4) and isopilocarpine 10^{-5} M and arecoline 10^{-7} M (7 animals 20 processes) was also without effect on the normal shrinkage of the ciliary processes

Intravenous *in vivo* injections of pilocarpine (11 animals 43 processes) or isopilocarpine (3 animals 15 processes) 2 mg/kg body weight 5 minutes before



Fi. 4

Arecoline added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Arecoline 10^{-4} M (6 animals 13 processes) Arecoline 10^{-5} M (6 animals 1/ processes) Arecoline 10^{-7} M (6 animals 12 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

have something to do with binding to cholinergic receptor sites The parasympathomimetic drug arecoline could also block the pilocarpine effect However the weak effect or absence of effect on this type of secretory activity caused by other parasympathomimetics such as acetylcholine carbacholine and arecoline seems to be at variance with a view of truly cholinergic receptor sites

Summing up it has been established that in order to produce an effect on the *in vitro* shrinkage of the ciliary processes both ends of the pilocarpine molecule seems to be of importance as well as their stereochemical position. With regard to the effect of pilocarpine on other epithelial transport systems *in vivo* and *in vitro* as well as its effect on accumulation *in vitro* by the ciliary processes of the eye the results from pilocarpine experiments with the present *in vitro* technique seems to be more in favour of a stimulated transport outwards to the stroma than of an inhibited transport inwards to the aqueous

The previously shown inhibitory effect of epinephrine (3) on the normal shrinkage of the ciliary processes was extremely difficult to establish Many preparations had to be discarded due to the anatomical disarrangement of the ciliary processes caused by the addition of epinephrine Using a rather high

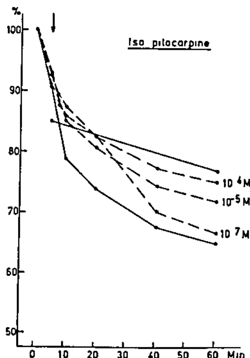


Fig 3

Isopilocarpine added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Isopilocarpine 10 4 M (4 animals 13 processes) Isopilo carpine 10^{-5} M (6 animals 18 processes) Isopilocarpine 10^{-7} M (4 animals 10 proces ses) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

inhibition of secretory activity This inhibition might be due to an inhibited transport inwards" to the aqueous or to a stimulated transport outwards to the stroma

In other secretory systems as for instance saliva or sweat or tear production pilocarpine has a stimulatory effect In *in vitro* transport experiments across the frog skin pilocarpine caused when applied to the outside a stimulatory effect on active sodium transport (8) In accumulation studies on rabbit eye ciliary processes it was shown that pilocarpine in low concentration stimulated the up take of iodopyracet Diodrast (9) an anion which like iodide is known to be transported out of the eye *in vitro* as well as *in vivo* (1 2 7)

The pilocarpine effect with the present *in vitro* technique clearly shows that the stereochemical molecular configuration of pilocarpine is of importance It has been demonstrated that the analogues of pilocarpine i e pilocarpidine and pilosine were without effect (6) as well as now also the stereoisomer isopilocar pine Furthermore the pilocarpine effect could be blocked by the parasympa tholytic drug atropine which would suggest that the pilocarpine effect might

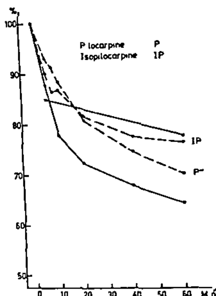


Fig 6

The animals injected intravenously *in vivo* with 2 mg/kg body weight of pilocarpine or isopilocarpine 5 minutes before perfusion Coordinates as in fig 1 Mean time shrinkage curves Curve P = pilocarpine (11 animals 43 processes) Curve IP = isopilocarpine (3 animals 15 processes) Continuous curve = mean standard curve with buffer solution, pH 7 4 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

isopilocarpine (10^{-5} M) as well as by *atropine* (10^{-7} M) and *arecoline* 10^{-7} *M*) It is suggested that the effect of pilocarpine might be due to its attachment to specifically oriented receptor sites in the ciliary processes

Isoproterenol (0 2 mg/ml) and norepinephrine (0 01 mg/ml) did not influence the normal shrinkage of the ciliary processes indicating that the epinephrine effect on the secretory activity might be a metabolic effect

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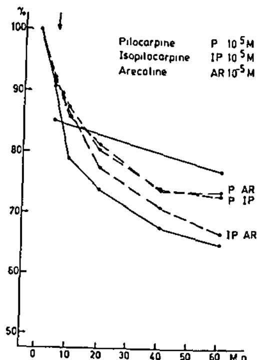


Fig 5

Combinations of pilocarpine isopilocarpine and arecoline added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Curve P + AR = Pilocarpine 10^{-5} M plus arecoline 10^{-5} M (5 animals 28 processes) Curve P + IP = Pilocarpine 10^{-5} M plus isopilocarpine 10^{-5} M (6 animals 19 processes) Curve IP + AR = Isopilocarpine 10^{-5} M plus arecoline 10^{-5} M (7 animals 24 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

concentration 10^{-4} M and a pH of 7 0 some successful experiments showed a blocking effect Moreover this effect could be abolished by the adrenergic metabolic inhibitor BW 61 43 (N isopropyl methoxamine) In the present experiments the effect of epinephrine could not be reproduced either by the alfa adrenergic norepinephrine or by the beta adrenergic isoproterenol These findings might be interpreted as an indirect confirmation of the previously presented suggestion that the effect of epinephrine on *in vitro* secretory activity of the rabbit eye ciliary processes could be a metabolic effect

Summary

The inhibition of the normal shrinkage of the ciliary processes *in vitro* by pilocarpine (10^{-5} M) could be abolished by the stereoisomer of pilocarpine

From the Helsinki University Eye Hospital
(Head Professor Salme Vannas M D)

FLUORESCEIN ANGIOGRAPHY OF THE OPTIC DISC AND THE PERIPAPILLARY AREA IN CHRONIC GLAUCOMA

BY

CHRISTINA RAITTA and TIMO SARMELA

The optic disc receives its vasculature entirely from the ciliary system as was confirmed by *Hayreh* (1962) in an extensive investigation In glaucomatous lesions of the optic disc a decreased vascularity of the disc might be expected This was in fact the main finding in *Hayreh s* (1967) fluoresceinstudy in glaucomatous patients

The peripapillary region has special anatomic features as has been demonstrated by *Michaelsson* (1954) and by *Alterman & Henkind* (1968) for the retina The choriocapillaris however is thought to be a continuos layer from the immediate peripapillary region to the ora serrata This uniformity however has been a subject of debate *Hayreh & Perkins* (1969) demonstrated experimentally deminished filling of the peripapillary choroidal vessels in acutely elevated i o pressure a result that might point towards the possibility of different functional zones

The present investigation was carried out in order to study the optic disc and peripapillary blood supply in chronic simple glaucoma and correlate the changes with visual field defects

R ce ed August 6th 1969

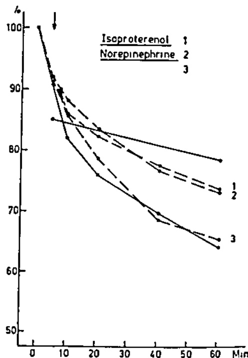


Fig 7

Isoproterenol and norepinephrine added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Curve 1 = isoproterenol 0 [illegible] mg ml (6 animals 15 processes) Curve 2 = norepinephrine 10 microg/ml (6 animals 15 processes) Curve 3 = norepinephrine 0 1 microg/ml (6 animals 12 processes) Continuous curve = mean selected standard curve with buffer solution pH 7 0 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

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Results

The vascularity of the disc was diminished in all our cases according to the degree of cupping (Fig 1) Circumcapillary choroidal atrophy was a constant finding even in the youngest patient aged 36 and only in one of the patients circumpapillary atrophy could be attributed to myopia

Peripapillary atrophy of the pigmentepithelium as sign of impaired choroidal circulation (Fig 2) was characteristic in cases with marked cupping and visual field defects (Fig 3) The atrophic zone formed a distinct region in the centre of the fundus though not always circular The retinal arterioles were narrow in correspondence to the degree of arteriolar sclerosis Retinal radial peripapillary capillaries were visible in one case (Fig 4) showing severe changes of the capillary structure neovascularization and congestion This patient had severe macular degeneration and a i o pressure level of about 40 mm Hg before treatment

Discussion

Fluoresceinangiography of the fundus of glaucomatous patients may be technically difficult especially in longstanding cases with senile or secondary opa

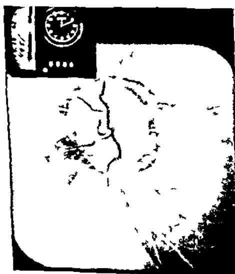


Fig 1

Diminished ascularity of the opt c disc and circumpapillary atrophy in a man aged 69 w th ch onic glaucoma The pre treatment pressure level was 40 mm Hg and an enlarged bl nd spot and a nasal step were found on perimetry

Material and Method

The present series (Table 1) consisted of 12 patients with chronic wide angle glaucoma and cupping of the disc Patients with i o pre treatment pressure levels $>$ 25 mm Hg pathologic diurnal curves and cupping of the disc were included in the series When angiography was performed i o pressure was $\leqq$ 25 mm in all cases Half of the patients were female and with one exception the patients were over 50 years of age The visual fields were plotted using the Goldmann apparatus for kinetic perimetry The central isopter 20° nasally using either test object I and intensity 2 or object 0 and intensity 3 was plotted using near correction and constant background illumination None of the patients had diabetes hematologic or severe hypertensive disease Fluorescein angiography was performed at 2 sec intervals by the method formerly described by *Raitta* (1968)

Table I
Data on 12 patients with wide angle glaucoma

Case	Age	Sex	The disc	Visual field
1	76	F	glaucomatous excavation	a part of temporal quadrant is left
2	73	F	glaucomatous excavation	a part of temporal quadrant is left
3	64	F	incipient glaucomatous excavation	an enlarged blind spot
4	36	F	incipient glaucomatous excavation	an enlarged blind spot
5	76	F	a temporal glaucomatous excavation	an enlarged blind spot
6	59	F	incipient glaucomatous excavation	normal
7	54	M	glaucomatous excavation	a Bjerrum scotoma
8	70	M	incipient glaucomatous excavation	normal
9	62	M	glaucomatous excavation	Bjerrum scotoma and nasal step
10	68	M	glaucomatous excavation	an enlarged blind spot and a nasal step
11	76	M	a temporal glaucomatous excavation	an enlarged blind spot
12	69	M	glaucomatous excavation	an inferior and temporal part of the field are left



Fig 4
Fluorescence pattern of a woman aged 76 with untreated glaucoma and a pressure level of 40 mm Hg and macular degeneration Marked visual field loss

have been found in choroidal as well as retinal peripapillary circulation (*Alterman & Henkind* 1968 and *Dollery* 1968)

Hemodynamics of the ocular circulation has some special features Because of the intraocular pressure venous capillary pressure is high approximately 2 mm Hg higher than the i o pressure Elevated i o pressure of any kind increases therefor the pressure in the veins The radial peripapillary capillaries being mainly veins seem to be very vulnerable to increased pressure Fluorescein angiographic changes of these capillaries were visible only in one of our cases with additional macular degeneration It might be concluded that the vascular lesion in glaucoma leading to nerve bundle lesion is choroidal and that only an arcuate angioscotoma seen early in glaucoma as well as in other conditions like papilledema (*Raitta & Vannas* 1969) can be produced by affection of the radial peripapillary capillaries Juxta and peripapillary atrophy of the pigmentepithelium was a constant finding and was most distinct in cases with severe cupping and functional loss Whether these changes are primary or secondary to elevated i o pressure is an interesting question Changes of the posterior and anterior uveal circulation might well be parallell This might be an explanation to the fact that glaucomatous changes may progrediate even if i o pressure levels are well controlled and to the socalled low tension glaucoma The degree of papillary and peripapillary changes corresponded with the de

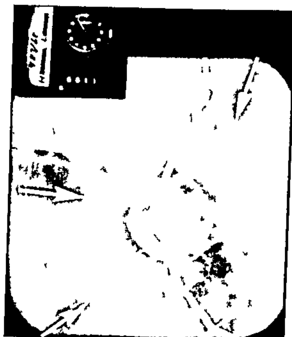


Fig 2
Peripapillary atrophy in a man aged 62 with a typical nerve bundle defect of the visual field Pre treatment pressure level 30 mm Hg

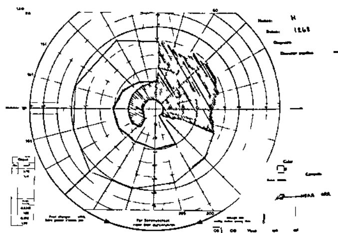


Fig 3
Visual field of patient described in fig 2

cities of the cornea lens and/or vitreous In *Hayreh s* (1967) study a diminished fluorescence of the disc was found to be typical No comments however were made upon peripapillary changes In experimentally elevated pressure changes

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A STUDY ON THE DISTRIBUTION OF ALKALINE PHOSPHATASE IN CERTAIN RETINAL LOCALES OF SNAKE AND VARANUS AND ITS FUNCTIONAL SIGNIFICANCE IN THE VISUAL PROCESSES

BY

H B TEWARI and H R TYAGI

Although histological accounts of reptilian eyes are available in the literature (*Walls* 1958) yet studies on the distribution of phosphatases and other enzymes on such retinae are lacking There is only a solitary report on the distribution of cholinesterases retinae of turtle and lizards (*Capurro et al* 1959) On the other hand other vertebrate eyes including humans have been extensively investigated from the point of view of distribution of phosphatases and other enzymes Also the distribution of cholinesterases and non specific esterases in the retinae of some mammals has been adequetely investigated (*Esila* 1963) The present contribution incorporates a detailed account of the distribution of alkaline phosphatase and discusses its metabolic roles in various retinal layers of snake and varanus Further the distributive patterns in the two animals have been also compared

Material and Methods

Eyes of snake and varanus obtained in living condition were cut into small pieces and were immediately fixed in 10% neutral formalin for periods vary

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gree of cupping and the severity of the visual field loss Advanced visual field loss was found to be a typical nerve bundle loss whereas early loss seen as en largement of the blind spot probably is an angioscotoma corresponding to the circulatory changes of the peripapillary area

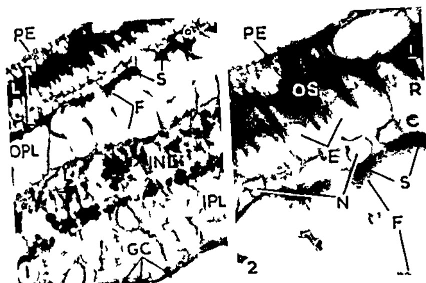
Summary

A fluoresceinstudy of the papillar and peripapillar region in 12 patients with chronic wide angle glaucoma and cupping of the disc is presented

Diminished vascularity of the disc and circumpapillary choroidal atrophy was a constant finding in the series In advanced glaucoma with severe func tional loss a peripapillary atrophic area was typical Severe vascular changes not only of the disc but of the juxtapapillary and peripapillary zone indicated that a zonular arrangement of the choriocapillaries might exist

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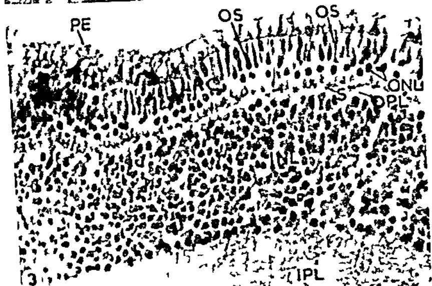


Fig 1

Retina of Snake Dist nguish the layers – pigmented epithelium (PE) layer of rods and cones (LRC) Outer nuclear layer (ONL) synapses (S) Fibers (F) Outer plexiform layer (OPL) Inner plexiform layer (IPL) and ganglion cell (GC) × 430

Fig 2

Higher magn fication of Fig 1 Note the intense alkal ne phosphatase activity in the outer segments of Rods and Cones (OS) D st nguish negative ellipsoid (E) and nuclear containing part (N) × 748

Fig 3

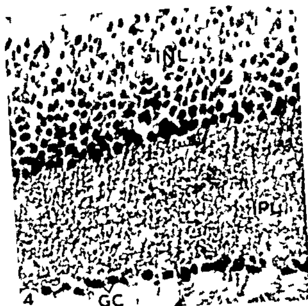
Retina of va anus I lent fy p gmented epithelium (PE) Distinguish posit ve layer of rod and on s (LRC) having posit ve outer segment (OS) and nuclei constituting outer nucle r laye (ONL) Positive synapses (S) in the outer most region of the negative oute plexiform layer (OPL) are also seen The latter s thinner than that of snake (compare OPL F g with OPL Fig 1) inner nuclear layer is thicker than that of snake s retina (compare INL Figs 1 and 3) × 380

ing from 4 to 6 hours Paraffin sections 10 μ thick after brief washing in distilled water were processed through Gomori s technique for alkaline phosphatase (cf *Pearse* 1961) Suitable controls were also simultaneously made

Results

In our preparations, both in control and normal identical staining in the pigmented epithelium prevents us from considering this layer as one of the sites of alkaline phosphatase activity However interesting results are provided by the layer of rods and cones (LRC Fig 1) In diurnal Colubrids to which the present material (Ptyas mucosus) belongs single and double types of cones are composed of outer segment ellipsoid and nuclear containing part (*Walls* 1958) Our preparations reveal that only the outer segments (OS Fig 2) are equipped with the enzymatic activity of a high order the ellipsoid (E Fig 2) and the nuclear containing part (N Fig 2) are totally negative It is interesting however to mention here that acid phosphatase activity has been seen in human cone ellipsoid by *Lassel et al* (1964) The notable point which must be stressed here is that the nuclei of all the cones constituting the outer nuclear layer (ONL Fig 1) are totally negative (see also N Fig 2) In a variety of tissues the nuclei are invariably alkaline phosphatase positive by Gomori s technique – a condition believed by some workers (*Holt s* 1959 1961 *Barka* & *Anderson* 1962 *Deane* 1963) to be artefectual in nature due to adsorption of lead ions or of lead or calcium phosphates by the nuclear sites even in the absence of any enzymic activity In the present case the absence of the alkaline phosphatase staining in all the nuclei can be advanced as one of the convincing arguments to disprove the assumption that nuclear sites always absorb reaction products or some constituents of the incubating medium of Gomori s technique and reveal false sites of the enzymatic activity In our experiments inspite of the presence of calcium ions all the nuclei of the rods and cones have failed to acquire staining Thus we believe that the localization of alkaline phosphatase in nuclei wherever it is seen represents the factual localization of the enzyme and is not due to any preparative factor

From the enzymatic point of view the other interesting sites besides the outer segments of the cones are the synaptic zones located at the bases of the cones in the outer most regions of the outer plexiform layer These areas representing the synapses between fibers of the bipolar horizontal and other cells of the inner nuclear layer and the bases of the cones are provided with intense enzymatic activity in our preparations (S Figs 1 and 2) In the inner region of the outer plexiform layer (OPL Fig 1) which is mainly constituted by traversing fibers of neurons of other layer the enzymatic activity is com





5

Fig 4

Note the intensely p sit ve Muller s fibers (arrows) running across the whole length f inner plexiform layer (IPL) Deeply stained ganglion cells (C C) are also seen

× 816

Fig 5

Distinguish a deeply sta ned positive zone at S above the positive ganglion cell (GC) The emain ng inne plex form layer is feebly stained (IPL) Further identify the positi nerve fibe s (NF) emerg ng from the ganglion cells and the associated positive synapses (S_1) × 1165

pletely lacking e g in some instances total lengths of fibers negative in nature (F Figs 1 and 2), are traceable across the outer plexiform layer However the inner nuclear layer, composed of closely packed bipolar cells (amacrine Muller and other types of bipolar cells) is intensely positive for alkaline phosphatase (INL Fig 1) On the other hand the inner plexiform layer provides a very faint diffused reaction (IPL Fig 1) Further the ganglion cells (GC Fig 1) constituting the inner most zone of the retina and the nerve fibers possess intense enzymatic activity

Varanus retina

The retina of Varanus monitor is essentially composed of the same layers as in the case of snake Only three variations are seen – firstly both rods and cones are found secondly the outer plexiform layer is greatly reduced and thirdly the inner nuclear layer is considerably thicker

As in the case of the snake s retina the pigmented epithelium of varanus also reveals identical staining in control as well as in normal preparations Con sequently this layer from the enzymatic point of view has been excluded from consideration The outer segments of both rods and cones in varanus are inten sely positive for alkaline phosphatase activity (OS Fig 3) and in this respect resembles the staining seen in the outer segments of the cones of snakes (com pare OS Figs 2 and 3) One significant departure in varanus s retina from that of snake s retina however is that all the nuclei of the rods and cones com posing the outer nuclear (ONL Fig 3) are invariably positive (compare ONL Figs 1 and 3) Such differences between the two retinae then provide an in teresting situation where we find that inspite of identical processing the nuclei in one case are negative and in other case positive This gives an added support to our view that nuclear localization of alkaline phosphatase by Go mori s technique is not artifectual in nature as feared by some workers but re flects the real enzymatic make up of the nuclei which give such a staining

In the peripheral portions of the outer plexiform layer (OPL Fig 3) which is considerably reduced in varanus as compared to that of snake (compare OPL Figs 1 and 3) the synaptic zones (S Fig 3) at the bases of the rods and cones are positive for alkaline phosphatase activity Thus we find that in both the retinae such synapses are identically equipped with the enzymatic activity (compare S Figs 1 2 3) The remaining portion of the outer plexiform layer (OPL Fig 3) is devoid of the alkaline phosphatase activity

The inner nuclear layer the zone much bigger than that of snake on the whole reveals enzymatic activity of a high order (INL Fig 3) The entire area is seen packed up closely by intensely positive neurons In the inner plexiform layer an interesting observations relates to the positive fibers traversing the en tire length of the area (arrows IPL Fig 4) These are probably Muller s fibers



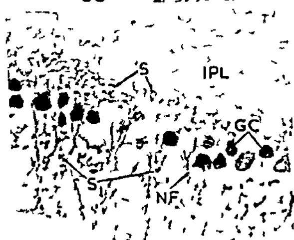


Fig 4
Note the intensely positive Muller's fibers (arrows) running across the whole length of inner plexiform layer (IPL) Deeply stained ganglion cells (GC) are also seen × 816

Fig 5
Distinguish a deeply stained positive zone at S above the positive ganglion cell (GC) The remaining inner plexiform layer is feebly stained (IPL) Further identify the positive nerve fibers (NF) emerging from the ganglion cells and the associated positive synapses (S_1) × 1165

Another very interesting situation seen in varanus retina relates to the area adjacent to the ganglion cells This area (S Fig 5) is constituted by synapses located immediately above the ganglion cells and possesses enzymatic activity of a higher order than the remaining portion of the inner plexiform layer (IPL Fig 5) The inner most layer is composed of ganglion cells and amacrine cells In our preparations these cells (GC Figs 4 and 5) have provided an intense *enzymatic reaction* It is also very interesting to note that the fibers emerging from these cells and their synaptic contacts with extra retinal fibers (S 1 Fig 5) possess enzymatic activity

Discussion

In the present study the outer segments of rods and cones the highly sensitive parts where the light strikes first and initiates nervous excitation reveal intense alkaline phosphatase activity In outer segments of rods and cones of pig rat and mouse the alkaline phosphatase activity has been also described (*Lessel et al* 1964) Now the question arises whether such enzymatic activity is in any way related to the initial visual processes undergoing in rods and cones? To seek a possible answer it is necessary first to understand that morphological and physiological conditions available in the outer segments of rods and cones Electron microscopical studies reveal that such regions are composed of closely packed flattened saccules which are derived from the plasma membranes In adult condition even some of the saccules remain connected with the plasma *membrane* throughout life in amphibian (*Lanzavecchia* 1960 *Lasansky & De Robertis* 1960 *Yamada* 1960 *Moody & Robertson* 1960 *Brown Gibbon & Wald* 1963) *Cohen* (1961 1963 1964) also note such a connection in the cones of pigeon grey squirrel and monkey The details of the initial steps in visual stimulation occuring in outer segments is still undecided There are two hypotheses – one believes that each saccule is a light *sensitive receptor* (*Wald* 1958) *the other postulates* that the whole outer segment is a photosensitive structure *Missotten* (1965) remarks that a difference in potential and difference in the ionic distribution existing between the inside and outside of a saccule is responsible for starting the initial steps in visual stimulation *Brown et al* (1963) believe that the special structure of the rim of the flattened saccule plays a part in the conveyance of the stimulation Since a saccule arises as a result of infolding of the plasma membrane a difference *in ionic distribution* as obtainable on the inner and outer sides of the plasma membranes is certainly expected on the inside and outside of the saccule as well since inside in infolded condition represents extracellular space and the outside the intracellular space In other words a situation akin to the biochemical makeup of the plasma membra

nes on the outer and inner sides of the saccules is available in the outer segments of rods and cones and such structures are expected to possess the substances and the metabolic activities of the same type and of the same order as are available in and around the plasma membrane Various types of phosphatases have been demonstrated at the neuronal and non neuronal plasma membranes (*Pothstein & Meier* 1948 *Derrick et al* 1953 *Clarkson & Maizels* 1952 *Tewari & Bourne* 1962a, 1963a b 1964 *Tewari & Sood* 1969 *Thakar & Tewari* 1967 *Tewari & Dabholkar* 1968) In this context therefore it would be quite reasonable to expect the presence of alkaline phosphatase at the membranes of the saccules which are nothing but the modified form of the plasma membranes *Tewari & Bourne* (1960a b 1961a b *Tewari et al* 1962c) in a number of studies have also demonstrated the presence of alkaline phosphatase other phosphatases and enzymes in another derivative of the plasma membrane namely the myelin sheath of sciatic nerve of rat the concentric ringes of which are thought to arise from the plasma membranes in the same fashion as the membranes of the saccules (*Adler* 1965) In the plasma membranes of excitable tissues the role of sodium and potassium ions through the mediation of phosphatases has been also fairly well established in the creation of action potential (*Danielli* 1952 *Tosteson et al* 1961 *Tewari & Bourne* 1960a b 1961a b 1962c *Pinner et al* 1964) – particularly a phosphatidic acid cycle as a sodium carrier involving ATP and ATPase has been postulated by *Hokin & Hokin* (1961) ATPase activity has been also seen in the outer segments of the retinae of many vertebrates (*Lessel et al* 1964) Since it has not yet been conclusively established whether ATPase is a simple enzyme or a combination of phosphokinase and a phosphatase (*Whittam* 1964) it can be suggested at the moment on the basis of present results that the phosphatases in general seem to be concerned with the permeability processes concerned with the ionic balances associated with creation of action potential Also *Tewari & Bourne* (1962a, 1963a b 1964) have found identical pattern of localization of alkaline phosphatase and ATPase at the neuronal surfaces and the role of phosphatase have been linked with the permeability processes The significance of energy phosphate compounds in active transport is also pointed out by the experiments in which application of such compounds on the inner membranes of red cells and nerve fibers revive the otherwise stopped active transport (*Caldwell et al* 1960a b *Caldwell & Keynes* 1957)

Against the background of these evidences our results demonstrating intense alkaline phosphatase activity in the zones of rods and cones possessing closely packed up structures derived from plasma membranes acquire considerable importance Our observations become more interesting when we consider that the initial factors for the origin of the stimulus like the inbalances of Na and K ions similar to the situations seen around the nerve membranes evoking impulses are available also around each saccule Since alkaline phosphatase is also

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Discussion

In the present study the outer segments of rods and cones the highly sensitive parts where the light strikes first and initiates nervous excitation reveal intense alkaline phosphatase activity In outer segments of rods and cones of pig rat and mouse the alkaline phosphatase activity has been also described (*Lessel et al* 1964) Now the question arises whether such enzymatic activity is in any way related to the initial visual processes undergoing in rods and cones? To seek a possible answer it is necessary first to understand that morphological and physiological conditions available in the outer segments of rods and cones Electron microscopical studies reveal that such regions are composed of closely packed flattened saccules which are derived from the plasma membranes In adult condition even some of the saccules remain connected with the plasma membrane throughout life in amphibian (*Lanzavecchia* 1960 *Lasansky & De Robertis* 1960 *Yamada* 1960 *Moody & Robertson* 1960 *Brown Gibbon & Wald* 1963) *Cohen* (1961 1963 1964) also note such a connection in the cones of pigeon grey squirrel and monkey The details of the initial steps in visual stimulation occuring in outer segments is still undecided There are two hypotheses – one believes that each saccule is a light sensitive receptor (*Wald* 1958) the other postulates that the whole outer segment is a photosensitive structure *Missotten* (1965) remarks that a difference in potential and difference in the ionic distribution existing between the inside and outside of a saccule is responsible for starting the initial steps in visual stimulation *Brown et al* (1963) believe that the special structure of the rim of the flattened saccule plays a part in the conveyance of the stimulation Since a saccule arises as a result of infolding of the plasma membrane a difference in ionic distribution as obtainable on the inner and outer sides of the plasma membranes is certainly expected on the inside and outside of the saccule as well since inside in infolded condition represents extracellular space and the outside the intracellular space In other words a situation akin to the biochemical makeup of the plasma membra

concerning specific and non specific cholinesterases in green and sand lizards and European turtle In green lizard retina there is no activity of specific cholinesterase in any layer except in inner plexiform layer and moderate activity in ganglion cells In sand lizard however there is moderate activity in outer plexiform layer amacrine cells and intense activity in inner plexiform layer and ganglion cells In European turtle there is no specific cholinesterase activity in outer and inner segments of visual cells Thus it is seen that the outer segments of snake and varanus which possess alkaline phosphatase activity as evidenced in the present study are devoid of specific cholinesterase activity The inner segment of snake is negative for alkaline phosphatase and thus resembles the retinae of green and sand lizards as far as specific cholinesterase localization is concerned However in the inner segments of varanus there is a moderate activity for alkaline phosphatase – this compares in favourably with the absence of cholinesterase activity in the same layer of green and sand lizards The outer nuclear layer is positive for specific cholinesterase in European turtle In our results in snake the layer is negative for alkaline phosphatase and in this respect resembles the similar layers in green and sand lizards which are negative for specific cholinesterases The outer nuclear layer of varanus is alkaline phosphatase positive which in turtle also possess specific cholinesterase activity In our material only the fiber traversing the outer plexiform layer demonstrates feeble alkaline phosphatase activity otherwise the layer is generally negative In turtle the same layer possess moderate specific cholinesterase activity which is negative for this enzyme in green and sand lizards The inner nuclear layer of turtle possess moderate activity for specific cholinesterase and the same layers in green and sand lizards are negative The ganglion cells in European turtle as well as in green and sand lizards are positive for cholinesterase These cells as already mentioned are positive for alkaline phosphatase in our materials In all the cases *Capurro et al* (1959) find complete absence of cholinesterases in the nerve fibers emerging from the ganglion cells In our study such fibers are positive for alkaline phosphatase

Summary

The study incorporates a detailed consideration on the distribution of alkaline phosphatase in certain retinal locales of snake and varanus and discusses the functional significance of the enzyme in the visual processes Although most of the constituents of the retinae like ganglion cells and other types of neurons have provided enzymatic activity of varying degree but the most interesting sites from the enzymatic point of view are the outer segments and synapses located at the bases of cones and rods and also above the ganglion cells A

present in these regions it seems quite reasonable to suggest that changes in the permeability through the mediation of alkaline phosphatase may be the factors *for initial stimulation in the outer segments* The present light microscopical study, however imposes on us a restriction to pin point the exact locale of alkaline phosphatase activity in the outer segments But such a handicap is unlikely to undermine our interpretation relating to the significance of alkaline phosphatase since both the views involving either the whole outer segment or only saccules are invoked at present Even if it is assumed that only saccules are concerned with the propagation of impulses then it may be pointed out that such structures fill up the outer segments so closely and completely that hardly any non saccular area is left and due to such tightly piledup alkaline phosphatase – positive seccular membranes the whole outer segment in a light microscopical picture would appear as if the enzymatic activity is present throughout the outer segment

The other interesting aspect of the present observations is the location of the enzymatic activity at various synaptic sites particularly at the bases of rods and cones and in the zone above the ganglion cells *Sjostrand* (1955) has clearly demonstrated that the dendrites of the cells penetrate and digitate into the enlarged terminal endings of the rods and cones to effect intimate synaptic contacts It is exactly at such sites that our results demonstrate intense alkaline phosphatase activity In a number of studies *Tewari & Bourne* (1962b 1963c) have suggested that alkaline phosphatase is concerned with the permeability processes across the synaptic membranes and we believe that the enzyme is playing the same role at these sites as well The same hold true for the synaptic contacts located above the ganglion cells

Walls (1963) has linked Muller s fibers to rivets which run through the whole thickness of the retina proper and bind its layer together and occupy a surprising amount of the total volume of the retina" Although previously the Muller fibers were though to be simply supporting in nature recent evidences based on the electrophysiological response of flashes of light (*Svaetichin et al* 1961) suggest that the fibers are associated with the metabolic and neuroregulatory roles In our preparations such fibers reveal alkaline phosphatase activity and therefore it is possible that the enzyme may be playing its role in metabolic and *neuroregulatory processess occurring in these fibers*

Regarding the significance of the distribution of alkaline phosphatase in ganglion cells and other neurons it may be briefly mentioned that the enzyme seems to be concerned with protein synthesis occurring in these cells as has been discussed earlier by us (*Tewari & Tyagi* 1967)

It seems interesting to see whether the alkaline phosphatase positive locales in our materials are also equipped with other enzymes in retinae of snake varanus and other animals As already mentioned there is hardly any enzymatic study in the retinae of *snake and varanus except that of Capurro et al* (1959)

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detailed consideration on the possible roles of alkaline phosphatase in the outer segments has been made with reference to the initial visual processes occurring in these areas The significance of the distribution of alkaline phosphatase at the synaptic sites has been also discussed with reference to the transmission of impulses

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SPONTANEOUS EXTRUSION OF SUBCONJUNCTIVAL CYSTICERCUS

BY

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Introduction

Cysticercus cellulosae is the larval form of Taenia Solium an intestinal para site Man is usually a definitive host of Taenia Solium but occasionally beco mes an intermediate host harbouring the bladder worm stage known as cysti cercus cellulosae The mode of infestation is by taking food and water con taminated with faecal matter containing ova A man harbouring the adult worm may autoinfect himself from unclean personal habits The envelope of the ova is dissolved in the upper intestinal tract releasing the embryo which by their hooklets penetrate into the wall of the intestine and enter the vascular and lymphatic plexus They are carried and get filtered in the muscles and viscera of the body They finally develop into cysticercus cellulosae a bladder worm which is composed of a head neck and a caudal vescicle The common sites are the eyes brain skin and muscles It gets calcified in a period varing from 5 years to 6 years after the death of bladder worm (*Chatterjee* 1967)

Ocular cysticercois is not a rare disease at Hyderabad Andhra Pradesh 32 cases of ocular cysticercois were noticed from January 1960 to April 1969 in our Institute Of which there were 23 cases from epibulbar region 2 from pal pabral conjunctiva 3 from the fornices one each from the lid orbit vitreous and anterior chamber Cases of spontaneous extrusion of subconjunctival cysti cercus has not been reported previously to our knowledge In the present case

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Fig 2
Spontaneous extrusion of the cyst – last phase



Fig 3
Photomicrograph of cysticercus cellulosae X 80 enlarged four times

Summary

37 cases of ocular cysticercosis were seen from January 1960 to April 1969 at the Institute of Ophthalmology Hyderabad A rare case of spontaneous extrusion of parasite from the subconjunctival space is reported

reported below the parasite came out spontaneously through the conjunctiva without any surgical intervention Probably a break was formed in the con junctiva, over the parasite due to necrosis

Case Report

A Hindu girl aged 5 years came to the Out patient Department on 20 12 1968 with her parents with a complaint of swelling and redness in right eye which was accidentally discovered 5 days ago There was no history of injury to the eye On examination of right eye the lids were found to be nlormal A certically oval reddish swelling was noticed in the upper nasal quadrant a few millimetres away from the limbus The conjunctiva was tense and congested over the swelling Swelling could not be moved over the underlying sclera Both the eye balls were found to be normal The case was diagnosed as subconjunctival cysticercosis

While taking the photograph the parasite began to come out through a small open ing from the centre of the swelling In a matter of 10 minutes the whole paratite came out with undulating movements (Fig 1 & 2) on its own accord leaving behind an emphy subconjunctival pocket The parasite by its macroscopic appearance showed all features of cysticercus cellulosae The conjunctival would healed in a few days leaving no residual swelling Histopathological examination of the cyst confirmed the diagno sis of cysticercus cellulosae (Fig 3)

Discussion

The diagnosis of the condition was made early by its site clinical features and by the age of the patient But the most important and rare manifestation was its spontaneous extrusion of the parasite from the subconjunctival space

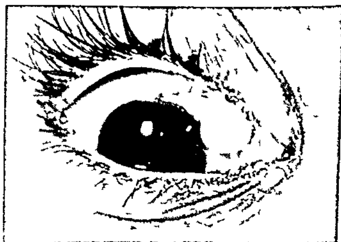


Fig 1
Spontaneous extrusion of the cyst

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From Odense County and City Hospital Eye Department
(Chief P M Møller M D)

DIVERGENCE PARALYSIS

BY

P M MØLLER

In neuro ophthalmological diagnosis an exact assessment of the restriction in ocular motility is often a decisive factor

During a period of 4 years we have seen 4 patients with motility disturbances which have been classified as divergence paralysis The complaints were consistent A sudden onset of diplopia for distance with a constant distance between the images whereas no diplopia was present at close and at reading with in approx 30 cm

Cases of this nature have not previously been reported in Scandinavian ophthalmological literature The case histories will be reported below and discussed in connection with a review of previous foreign publications on this subject

Since *Parinaud* in 1883 reported the first case of divergence paralysis it has been discussed at intervals whether in fact there is a centre for active ocular divergence

From a phylogenetic point of view it might be imagined that a divergence centre would develop as the antagonist of a convergence centre *Bruce* (3) has been one of the most ardent proponents of the view that divergence paralysis must be due to an affection of a given active divergence centre

This theory has found support in the experiments of *Adler* (1) Conducting electrical impulses from human lateral rectus muscles he found these impulses to become intensified in immediate connection with divergences He assumed that this increase in tonus issued from a divergence centre Divergence has been induced in monkeys by stimulating the frontal cerebral cortex but this has not been possible in man

Received February nd 19 0

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II S R P 210131

A male aged 3? with a history of complaints through 2 years in the form of periodical pain in the cervical spine towards the cr nial base accentuated on turning the head One year ago he had suddenly developed *convergent strabismus* with blurred vision and diplopia of a few days *duration* Still shooting pain at the back of the neck *at times with slight dysphagia* Shortly before admission again sudden permanent convergent strabismus with diplopia.

Visual acuity 6 6 in both eyes emmetropia

Alternating convergence strabi mus without restriction of motility and without ny stagmus At a distance of 3 m uncrossed double images *abolished by prism 20 p d* base out The *double images were of the same distance* when gazing to the right and left At 30 cm fusion without any movements of adjustment Caloric test by the Hall pike method Normal reactions with full abduction to both sides

Ophthalmoscopic appearances normal no papilledema

Tomography revealed a large rhinopharyngeal tumour extending into the sphenoid sinus and destroying the dorsum of the sella and right *down to the foramen magnum*

Biopsy from the rhinopharynx failed to show definite tumour

Autopsy revealed a large tumour at the base of the skull invading the sphenoid bone (rhinopharyngeal carcinoma)

III L.S R 060459

A boy aged 6 years who for the past 6 months had been *falling incessantly* and had *sustained several cranial traumas According to his mother* the boy had changed mentally and *now had spells of fear* She had several times observed convergence which had again disappeared Constant strabismus during the past two weeks before admission.

Visual acuity 6 6 in both eyes emmetropia

Severe convergent strabismus completely free motility No nystagmus Reported constant *uncrossed diplopia at 1 m when tested with red glass Fusion at 15 cm and fusion* at 6 m with a prism 30 p d base out

Ophthalmoscopy revealed incipient papilledema on both sides

Ventriculography showed a space filling lesion in the pons presumably a glioma This was confirmed at operation

Post mortem examination of the brain showed the tumour to be an astrocytoma of the pons

IV E O M 140833

A female aged 35 Dur ng the past 2 years she had been suffering from occipital headaches In addition she experienced difficulty in controlling her left arm and sudden tw tch ngs of the left leg Two weeks *before* she was seen here she developed d pl pia for distance most pronounced when she was tired

When first seen, she did not have diplopia within 1 metre Motility entirely normal No nystagmus

Visual acuity 6 6 in both eyes emmetropia

Ophthalmoscopy showed b lateral papilledema *of 4 5 dioptres*

A few days later we observed ocular movements that might indicate bilateral abducens pares s w th d stinctly reduced motility

An ther exam nat on ? m nths after the onset of the symptoms and signs and one week afte the abdu ens paralysis had been observed again showed normal motility int all li ect ons but the red glass test at 3 m as well as examination in the syn pt ph r in Zer p sit on sh wed uncrossed dipl pia w th the same distance between

Scobee & *Green* (11) have suggested that there is a vergence centre in the form of a convergence centre only "since exophoria and esophoria behave not as independent entities but rather as varying degrees of the same entity

Chamlin & *Davidoff* (5) collected 15 cases of divergence paralysis Of these patients 14 had elevated intracranial pressure Eight were found to have tumours of the posterior fossa whereas in 7 no definite tumours were demonstrable These authors therefore, suggest that despite the absence of papilledema patients with divergence paralysis should be suspected of elevated intracranial pressure

In a paper on bilateral abducens paralysis *Bedrossian* (2) set up strict criteria for classifying a case as divergence paralysis Watching ocular movements is not enough The abduction has to be measured, and in pure cases (i e in the absence of 6th nerve palsy), it must exceed adduction by 10°

According to Bedrossian s studies the abduction is 60° (measured as a normal field of fixation)

Nystagmus must not occur in the extreme positions if a case is to be diagnosed as divergence paralysis as this is taken to mean that the muscle is paretic.

In Bedrossian s opinion many reported cases of divergence paralysis have not been pure while on the other hand a number must have been overlooked considering the modest space devoted to divergence paralysis in the neuro ophthalmological literature

The etiology of divergence paralysis is unknown It has been observed in cases of poisoning infections disseminated sclerosis(hypoxic states and in the presence of elevated intracranial pressure (*Chamlin* & *Davidoff*)

Case Reports

I N A M 160546

A male aged 19 Through the past year he had been suffering from diffuse head aches and occasional diplopia For the past few months constant diplopia for distance Stated that he could read without difficulty

Visual acuity 6/6 in both eyes emmetropia

At 3 m esotropia of 20 prism dioptres No movement of adjustment, orthophoria at 30 cm At 20 cm distinct exophoria

Reported uncrossed diplopia with the same distance between the images at ° m to the sides as well as up and down In extreme positions *delicate nystagmus*

Ophthalmoscopy showed papilledema at 1 dioptre in both eyes

Ventriculography revealed a tumour in the posterior crania fossa

Operation disclosed a tumour suggesting a medulloblastoma in the pons Estimated length 6 7 cm transverse diameter approx 5 cm The tumour did not involve the 4th ventricle Part of the right cerebellar hemisphere and tonsil were removed The tumour was infiltrating the brachium pontis

Histological diagnosis Medulloblastoma

Died in his home No post mortem examination of the brain

II S R P 210131

A male aged 37 with a history of complaints through 2 years in the form of periodical pain in the cervical spine towards the cranial base accentuated on turning the head One year ago he had suddenly developed convergent strabismus with blurred vision and diplopia of a few days duration. Still shooting pain at the back of the neck at times with slight dysphagia Shortly before admission again sudden permanent convergent strabismus with diplopia

Visual acuity 6 6 in both eyes emmetropia

Alternating convergence strabismus without restriction of *motility and without nystagmus* At a distance of 3 m uncrossed double images abolished by prism 20 p d base out The double images were of the same distance when gazing to the right and left At 30 cm fusion without any movements of adjustment Caloric test by the Hallpike method Normal reactions with full abduction to both sides

Ophthalmoscopic appearances normal no papilledema

Tomography revealed a large rhinopharyngeal tumour extending into the sphenoid sinus and destroying the dorsum of the sella and right down to the foramen magnum

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Severe convergent strabismus completely free motility No nystagmus Reported constant uncrossed diplopia at 1 m when tested with red glass Fusion at 15 cm and fusion at 6 m with a prism 30 p d base out

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IV E O M 140833

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When first seen, she did not have diplopia within 1 metre Motility entirely normal *No nystagmus*

Visual acuity 6 6 in both eyes emmetropia

Ophthalmoscopy showed bilateral papilledema of 4 5 dioptres

A few days later we observed ocular movements that might indicate bilateral abducens paresis with distinctly reduced motility

An ther examination ? months after the onset of the symptoms and signs and one week after the abducens paralysis had been observed again showed normal motility rt ll lre tions but the red glass test at 5 m as well as examination in the synpt ph re n Zero po it n showed uncrossed d plopia with the same distance between

the images in all directions Simultaneous perception and fusion at + 26 prism dioptres in the synoptophore and when examined at 20 cm

Ventriculography failed to show any definite abnormality

Right sided carotid angiography gave rise to a suspicion of a space filling lesion in the right hemisphere

The patient developed a severe mental disorder and committed suicide

Post mortem examination of the brain revealed an astrocytoma in the semioval centre in the right parietal region extending down towards the basal ganglia and through the corpus callosum towards the left side Brain stem and cerebellum normal The cut sections showed no abnormalities

Histological diagnosis Astrocytoma primarily affecting the right parietal region

All our 4 patients were fully awake and cooperative when examined

All were examined both with and without cycloplegia The angle of deviation did not change in complete paralysis of accommodation

Discussion

Our Cases I II and III had what I should call pure divergence paralysis

Case I had delicate nystagmus in extreme abduction to both sides I cannot accept Bedrossion s view that this is a sign of abducens paralysis when considering how often delicate nystagmus in extreme lateral gaze is found in normals

All our patients had confirmed tumours of the posterior fossa either in the pons or else as in Case II neoplastic masses infiltrated the cranial base as far as the sphenoid bone

Godtfredsen (7) never observed divergence paralysis among 240 patients with malignant tumours of the rhinopharynx

Our Case IV differed somewhat from the others When first seen she did not arouse any suspicion of divergence paralysis At 1 m there was no diplopia in the differentiated red glass test

A few days later however there was distinct limitation of abduction to both sides and in another week we found at 3 m distinct uncrossed diplopia which disappeared at 20 cm

In my opinion such a transient abducens paralysis could not rule out divergence paralysis in our Case IV cf *Walsh* Clinical Neuro ophthalmology (17)

We found definite divergence paralysis repeatedly but the varying transient limitations of abduction I interpret as mild abducens paresis subsequent to acute elevation of intracranial pressure Not uncommonly such paresis is seen in conditions involving elevated intracranial pressure As already mentioned there was bilateral papilledema of 4 5 dioptres

Our 4 patients had the following findings in common

(1) Diplopia uncrossed for distance

(2) They volunteered the information that *at close they were not bothered by* diplopia

(3) A malignant intracranial tumour of the posterior fossa as the underlying cause

On this basis nothing can be concluded concerning the cause of the divergence paralysis except that pressure upon or against the brain stem must have been contributory but the exact localization of a presumed divergence centre cannot be deduced

The pons and the midbrain must be the site to look for the cause of the disease (int. al *Lyle* (9)) It is of less importance to ascertain whether the lesion affects a given centre or else the posterior longitudinal fascicle or the medial longitudinal fascicle. It must be admitted that the intimate association between the oculomotor trochlear and abducens nuclei in coordinating ocular movements must be extremely vulnerable by a tumour in the pons and midbrain

On the whole the problem concerning divergence paralysis remains unsolved It is given little attention in neuro ophthalmological diagnosis In the event of a suddenly arising convergent squint especially in patients with neurological signs examination for this peculiar anomaly may be done In most instances the differential diagnosis ought to be easy if only the patients are able to co operate

Definite criteria of the diagnosis must be

I Acute onset of homonymous permanent diplopia with a constant distance between the images in all positions especially in the horizontal plane

II Esotropia for distance Fusion at approx 25 30 cm

Frequently we are apt to assume merely that a previously latent convergence due e g to a trauma has become manifest Without performing the necessary diplopia test together with a fusion test at about 25 30 cm it is not possible to arrive at the correct diagnosis viz divergence paralysis

A situation which may simulate divergence paralysis is esotropia arising as a result of contracture of the internal rectus muscle during the course of long lasting abducens paralysis During the remission and upon return of normal abducens function the patient may exhibit esotropia with constant uncrossed double images for distance According to *Bynke* (4) this is not entirely rare especially not in young children

It is also of importance in order to arrive at the diagnosis that any patient complaining of diplopia should be examined not only by the usual conventional differentiated red glass test within about 1/2 m. Divergence paralysis usually does not manifest itself in uncrossed diplopia until at a distance of perhaps up to 5 m

Patients having convergence spasms and divergence insufficiency which may simulate divergence paralysis are often patients without serious neurological

the images in all directions Simultaneous perception and fusion at + °6 prism dioptres in the synoptophore and when examined at 20 cm

Ventriculography failed to show any definite abnormality

Right sided carotid angiography gave rise to a suspicion of a space filling lesion in the right hemisphere

The patient developed a severe mental disorder and committed suicide

Post mortem examination of the brain revealed an astrocytoma in the semioval centre in the right parietal region extending down towards the basal ganglia and through the corpus callosum towards the left side Brain stem and cerebellum normal The cut sections showed no abnormalities

Histological diagnosis Astrocytoma primarily affecting the right parietal region

All our 4 patients were fully awake and cooperative when examined

All were examined both with and without cycloplegia The angle of deviation did not change in complete paralysis of accommodation

Discussion

Our Cases I II and III had what I should call pure divergence paralysis

Case I had delicate nystagmus in extreme abduction to both sides I cannot accept Bedrossion s view that this is a sign of abducens paralysis when considering how often delicate nystagmus in extreme lateral gaze is found in normals

All our patients had confirmed tumours of the posterior fossa either in the pons or else as in Case II neoplastic masses infiltrated the cranial base as far as the sphenoid bone

Godtfredsen (7) never observed divergence paralysis among 240 patients with malignant tumours of the rhinopharynx

Our Case IV differed somewhat from the others When first seen she did not arouse any suspicion of divergence paralysis At 1 m there was no diplopia in the differentiated red glass test

A few days later however there was distinct limitation of abduction to both sides and in another week we found at 3 m distinct uncrossed diplopia which disappeared at 20 cm

In my opinion such a transient abducens paralysis could not rule out divergence paralysis in our Case IV cf *Walsh* Clinical Neuro ophthalmology (17)

We found definite divergence paralysis repeatedly but the varying transient limitations of abduction I interpret as mild abducens paresis subsequent to acute elevation of intracranial pressure Not uncommonly such paresis is seen in conditions involving elevated intracranial pressure As already mentioned there was bilateral papilledema of 4 5 dioptres

Our 4 patients had the following findings in common

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MEDIASTINOSCOPY WITH LYMPH NODE BIOPSY CARRIED OUT IN PATIENTS WITH ENDOGENOUS UVEITIS OF UNKNOWN ETIOLOGY

BY

VAGN NORDENTOFT M D and POUL MARTIN MØLLER M D

The presumed etiology of endogenous uveitis has varied very considerably throughout the times

Kaufmann (?0) wrote in 1966 The main problem in the diagnosis of uveitis is that it is almost never possible to find the cause in a given case

In the last 15 20 years the interest in sarcoidosis as an etiological factor has been increasing but in spite of the numerous biopsy methods that are avail able in suspected sarcoidosis this diagnosis is only rarely obtained in cases of endogenous uveitis The frequency of sarcoidosis in different surveys is shown in Table I It is in the literature generally stated that the frequency is approxi mately 4 per cent

The results of the present investigation are suggestive of a constant localiza tion of sarcoid granuloma in the mediastinal lymph nodes in sarcoidosis (18)

In 1959 *Carlens* (15) described mediastinoscopy a method which permits ex ploration of the superior mediastinum by palpation inspection and biopsy This

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Summary

Four patients with signs of divergence paralysis are analysed The author emphasizes the importance of a careful examination for diplopia for distance as well as for near in patients with sudden onset of convergence strabismus

In all our four cases intracranial tumours were the underlying cause Convergence spasms which may simulate divergence paralysis often represent a condition in which no neurological signs are manifest

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divided by blunt dissection and a tunnel is made with a finger in the loose tissue in front of the trachea into the mediastinum It is usually easy to expose the trachea down to the bifurcation The area is palpated enlarged lymph nodes are usually readily palpable The mediastinoscope is introduced (Fig 1) and via the scope the mediastinal tissue especially the lymph nodes *may* be dissected and biopsied Histological examination has been carried out on the biopsy material together with examination for TB by guinea pig culture

Material

The material is partly selected inasmuch as all our patients are referred to the department from practising ophthalmologists who themselves have treated the slight cases Prior to the commencement of the study however we had asked that as many cases of uveitis as possible should be referred to the department

Mediastinoscopy has not been carried out on 8 children below the age of 10 years and not on 7 patients above 70 years of age Neither has it been carried out on 13 patients where the etiology was known on admission (Table 4) Finally it was not carried out on a further 3 patients by mistake

There have been 108 cases of endogenous uveitis in the whole period the 77 have been subjected to mediastinoscopy

No lymph nodes were found in 3 cases during the attempt at mediastinal

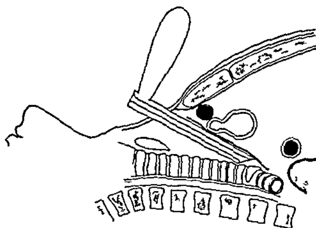


Fig 1
Schematic lateral view of mediastinoscope introduced in the correct plane beneath the pretracheal fascia.

Table 1
The frequency of sarcoidosis in surveys of uveitis in the literature as from 1950

Author	Year	Type of material	Total Patients	Number of sarcoidosis cases
Bjorkenheim[1]	1952		150	0
Vesterdal[2]	1952	Endogenous uveitis	350	23
Woods et al[3]	1954	Chorioretinitis	301	12
Alvaro[4]	1954		175	0
Bennett[5]	1955	Primary uveitis	332	7
Stanworth et al[6]	1957	Endogenous uveitis	197	2 + 1 doubtful
Perkins[7]	1961	Generalized uveitis	1718	55
Woods et al[8]	1961	Endogenous uveitis	723	19
Bergaust[9]	1962		255	1
Giles[10]	1963	Anterior uveitis in children under 16 years of age	16	9
Leira[11]	1965	Endogenous nonpurulent	420	1
Bergaust[12]	1966	Patients of more than 50 years of age	121	1
Haut[13]	1966	Endogenous 718 exogenous 132	850	7 + 4 doubtful
Hemmes[14]	1968	Acute anterior uveitis	386	not stated

procedure has proved to be safe and of great clinical importance in various intrathoracic conditions e g bronchogenic carcinoma and sarcoidosis

The method has since in many centers become a routine examination inasmuch as it gives more positive findings than biopsy carried out according to the method of Daniels (16 17 18) or with biopsy of other organs (18) in patients suspected for sarcoidosis

Since 1964 we have carried out mediastinoscopy with lymph node biopsy from the superior mediastinum in patients with endogenous uveitis where we have no known etiology in order to find out whether the frequency of sarcoid iritis in unselected cases is larger than found until the present

Method

Mediastinoscopy with lymph node biopsy is carried out under general anaesthesia The anterior wall of the trachea is freed throughout a 3 4 cm long transversal incision at the level of the suprasternal notch The pretracheal tissue is

Table 2

Distribution of 108 cases of endogenous uveitis according to type

Diagnosis	— Mediastinoscopy	+ Mediastinoscopy — Sarcoidosis	+ Mediastinoscopy + Sarcoidosis	Total
Uveitis chron bilat	10	24	10	44
Uveitis acute bilat	3	5	4	12
Uveitis chron unilat	10	14	0	24
Uveitis acute unilat	8	20	0	28
	31	63	14	108
Total				

biopsy In these 3 patients the histological diagnosis were respectively thymus tissue, thyroid tissue and fat tissue

Complications

There have only been a few complications with the procedure in our material One patient had postoperatively a temporary paralysis of the left recurrent nerve In one patient there was haemorrhage from a small vein which however ceased on tamponade In another a slight pneumothorax of no great importance occurred

Results

Of the 77 patients that had been subjected to mediastinoscopy a histological picture compatible with sarcoidosis was found by histological examination in 14 I e 13 per cent of the whole series 18 2 per cent of those who were subjected to mediastinoscopy, and 21 2 per cent of all the bilateral cases

Table 2 and 3 show the distribution of the forms of uveitis in the material It must however be mentioned that in 12 patients ophthalmoscopy was not possible either owing to a small synechial bound pupil or owing to complicated cataract These patients are classified as panuveitis All the patients with sarcoidosis could be subjected to ophthalmoscopy In the 63 patients who had been subjected to mediastinoscopy without sarcoidosis being found the etiology was only discovered in 4 One was a patient where TB was found on cultivation from the biopsy material One had toxoplasmosis with increasing titer with complement fixation test and dye test one had temporal arteritis (Horton) verified by biopsy and one Mb Reiter In all the etiology was thus found in 31 patients (Table 4) which corresponds to 28 7 per cent of the whole material

The Sarcoidosis Group

The 14 patients where the histological examination showed by typical epithelioid cell granuloma compatible with the diagnosis sarcoidosis were distributed with regard to age between 15 and 70 years 8 of the patients were more than 50 years of age There were 8 women and 6 men As can be seen from table 2 all had bilateral uveitis

The 4 patients classified as acute were admitted 10 14 days after the occurrence of the first symptoms and were healthy after approximately one month

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Table 4

Etiological factors in 108 patients with endogenous uveitis

— Mediastinoscopy	Morbus Bechterew	2
	Ulcerous Colitis	1
	Rheumatic Fever	1
	Influenza C.	1
	Keratoiritis	1
	Lues Cong (active)	1
	Ophthalmia Sympatica	1
	Rheumatoid Arthritis	1
	Morbus Still	2
	Varicella	1
	Ophthalmic Zoster	1
+ Mediastinoscopy	Temporal Arteritis (Horton)	1
	Morbus Reiter	1
	Toxoplasmosis	1
	Tuberculosis	1
	Sarcoidosis	14
Total		31

None of these have suffered from recurrence since The period of observation is more than two years All 4 were men between 30 and 50 years of age

All the 10 classified as chronic had symptoms of more than 1 month s duration prior to admission and the majority had had previous attacks of *uveitis* All have since been controlled for more than 6 months because of continuous or recurrent inflammation

One patient had had recurrent uveitis for more than 20 years and had been admitted to various ophthalmological departments without the etiology having previously been found

All of the patients had similar to those without sarcoidosis had topical steroid treatment from the practising ophthalmologist for a shorter or longer period prior to admission A few had previously received systemic steroid treatment in smaller doses The clinical ophthalmological picture might have been affected by this treatment

We have not during the study had the impression that the group with sarcoidosis showed any characteristics compared with the patients not suffering from this disease

Mutton fat K P were equally distributed between the two groups (in ap

Table 3

Distribution of 108 patients with endogenous uveitis according to localization

Diagnosis	— Mediastinoscopy	+ Mediastinoscopy — Sarcoidosis	+ Mediastinoscopy + Sarcoidosis	Total
Uveitis ant	9	15	1	25
Uveitis post	3	3	0	6
Panuveitis	19	45	13	77
Total	31	63	14	108

Symptoms from other Organs

Only a few of the patients had symptoms from other organs 3 of the patients had slight uncharacteristic symptoms of the joints

One patient was primarily admitted to the neurosurgical department for ob servation for an intracranial tumour owing to intracranial calsification around the sella and impaired vision Daniels biopsy had previously been performed on this patient owing to radiologically demonstrated enlarged hilar lymph nodes but this had been negative

One patient had Heerfordt s syndrome on admission

X ray examination of the lungs initially showed enlargement of the media stinal lymph nodes in 7 patients In an additional 2 patients hilar changes were found by subsequent tomography No radiological changes of the thorax were found in the remaining 5 patients

None of the patients with demonstrable involvements of the mediastinal lymph nodes had had respiratory tract symptoms

Laboratory Tests

7 of the patients had a moderate increased sedimentation rate (17 44 mm/H) Of these 2 had a slightly increased Alpha serum globulin whilst one with a normal sedimentation rate also had the same increase

The Mantoux test was positive in 5 patients

Serum calcium was normal in all the patients

We have not used Kveim s skin test as all the patients were put onto systemic steroid treatment immediately after the mediastinoscopy had been carried out (19)

Treatment

All the patients were treated with corticosteroids both topically and syste mically

We have not seen steroid induced increase in the intraocular pressure neither in the group with sarcoidosis nor the others

Comments

We consider that Carlens introduction of mediastinoscopy with lymph node biopsy has made it possible for the ophthalmologist together with the endo scopist to find nearly all cases with uveitis caused by sarcoidosis

proximately 50 per cent) and were mainly seen in patients who had only been on steroid treatment for a short period prior to admission

Nodules of the iris were seen in 2 of the 14 sarcoidosis patients and in 6 of the remainder

Neither have we had any definite impression of a difference between the sarcoid- and the non sarcoid group following ophthalmoscopy and three mirror prism examination We have seen dilated veins periphlebitis perivenous nodules exudations and haemorrhages in both groups Similarly we have seen vitreous opacities, particularly "snowballs" in the periphery in both groups

We have counted the patients with iris nodules perivenous nodules and/or snowballs in the bilateral cases in both groups after the study had been finished and a clear difference could then be seen (table 5)

Typical candle wax exudates have only been seen in one patient who had sarcoidosis

None of the patients with sarcoidosis had conjunctival or scleral involvement. Neither has keratoconjunctivitis sicca been seen

10 of the patients were admitted during the first attack This has in all probability contributed to the fact that the ophthalmological clinical picture in this group has been less distinct and with only few complications

Two of the sarcoid group have developed secondary glaucoma which could be regulated by epinephrine bitartrate

The patient who had suffered from recurrent uveitis for more than 20 years has now severely impaired visual acuity (3/60 on the best eye) partly owing to complicated cataract but especially owing to severe vitreous opacities

One man of 55 years was admitted after only having slight symptoms of uveitis for 14 days Despite intensive systemic steroid treatment he developed severe bilateral panuveitis retinal detachment in one eye with severe vitreous haemorrhages After a two years period of observation and systemic steroid treatment he still suffers from uveitis with recurrent attacks

Table 5

The presence of iris infiltrations snowballs and/or previous nodules in patients with acute or chronic bilateral uveitis (66 cases)

	Positive findings	Total number	%
Patients with sarcoidosis	8	14	57.1
Patients without sarcoidosis	9	42	21.4

Symptoms from other Organs

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We consider that Carlens introduction of mediastinoscopy with lymph node biopsy has made it possible for the ophthalmologist together with the endoscopist to find nearly all cases with uveitis caused by sarcoidosis

The examination is not difficult to perform and is rather harmless with on a few and slight complications

In a series of 2500 cases from Sweden and Denmark (21) very few complic tions occurred 3 cases had recurrent nerve paralysis One had rupture of tl bronchus resulting from biopsy of a carcinoma Slight haemorrhage can also o cur however, this can be easily stopped by tamponade Pneumothorax can al develop

The procedure should be carried out by an experienced endoscopist workin in cooperation with a thoracic center

There are only a few contra indications

The procedure can be difficult to carry out on smaller children owing to th lack of space It should not be carried out where a prior diagnosis exists an neither should it be done where other sites of the affection are more readil available and from which it is easier to obtain biopsy material as for exampl with palpable lymph nodes Neither should the procedure be carried out n patients where there is doubt as to whether or not they are able to stan general anaesthesia (18)

The advantages with the method are that it is possible to obtain an earlie and more certain diagnosis than by Daniels biopsy and in addition the proce dure is more safe to perform (18)

The certainty of the diagnosis is as great as it is possible to obtain at present time namely the histological examination

A diagnosis of sarcoidosis can be obtained only by a study of the patient's case as a whole the history and the results of clinical radiographical bacterio logical and laboratory investigations Confirmative histological evidence is de sirable and should be sought whenever possible (18)

Pathologically the typical lesion is the so called epithelioid cell granuloma which independently of the location presents the same histological picture The granuloma which is characteristic and constitutes a necessary basis for a de finite diagnosis consists of clusters of epithelioid cells surrounded by a nar row rim of lymphocytes Giant cells of both the Langhans and foreign body types are frequently present The histological appearance is similar to that of tuberculosis but there is no central necrosis and tubercle bacilli are absent (Fig 2)

The histological appearance of non caseating epithelioid cell granuloma is most often due to sarcoidosis These histological features however are also common to a large group of granulomatous infectious diseases including tuber culosis leprosy syphilis and others Therefore the histopathological reaction must always be interpreted in conjunction with the clinical features of the spe cific case

In relation to this it should be noted that one of our patients with bilateral uveitis had sarcoidosis like epithelioid cell granuloma in the histological sec



Fig 2

Microscopic section of mediastinal lymph node showing characteristic histological pattern of epithelioid cell *granuloma containing* multinucleated cells no evidence of necrosis (Hematoxylin and eosin × 100)

tion and normal conditions in the chest radiography Cultivation from the lymph node biopsy demonstrated however growth of T B bacilli without the patient showing other signs of T B thus gastric lavage showed no growth of TB bacilli

In three other patients with bilateral uveitis epithelioid cells suggestive of sarcoidosis were found during histological examination However these cells did not show the typical granuloma arrangement and therefore these 3 patients were not included in the survey

It can be seen from table 1 that the frequency of sarcoidosis varies enormously as th etiological factor of uveitis None of the investigators however have been particularly interested in obtaining the diagnosis sarcoidosis The figures cannot be compared without reservation particularly owing to the different methods of examination used in order to obtain the diagnosis sarcoidosis A negative biopsy according to the method of Daniels or the absence of hilary lymphadenopathy during x ray examination does not exclude by any means the sarcoidosis as the cause of a uveitis

It is interesting that 5 of our 14 patients with sarcoidosis had normal chest

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lary lymph nodes and among these microscopy demonstrated in 14 cases giant cell granuloma as an expression of sarcoidosis

No serious complications followed the mediastinoscopy which was performed under general anaesthesia by the chest surgeons

X ray of the chest showed definite normal conditions in 5 of the patients in whom mediastinoscopy with biopsy demonstrated sarcoidosis

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radiographs *Jepsen* (22) reports that he in a series of 81 patients with sarcoidosis found that 9 of the patients had normal findings with radiological examination of the thorax similar to the cases referred to here

The frequency of sarcoidosis stated in literature varies considerably (23)

In Denmark 5 new cases per 100 000 inhabitants are reported annually It is considered that approximately 80 per cent of the cases are reported (24) Our department serves a population of approximately 250 000 Compared with the above it would mean that there during a 4 year period, should be at least 63 new cases of sarcoidosis *James* (25) has found that approximately 20 per cent of the cases of sarcoidosis have uveitis which again would mean that we in the period under study should have found approximately 12 13 This theoretical figure corresponds well to our result The fact that *Scadding* (19) finds that approximately 10 per cent of all the cases of sarcoidosis commence with uveitis, also corresponds well to our results Our series is small but it is remarkable that so few patients have had general symptoms Similarly it has also been remarkable that all the cases with a few exceptions have only presented vague symptoms None of the patients with sarcoidosis had such severe and characteristic findings in the anterior part of the eye as described by *Woods* (26) but this may be due to early steroid treatment which as stated by *James* (27), results in a striking improvement in patients who are treated within one or two years of the onset of the disease

Based upon the cases we have seen we must agree with *Witmer* (28) that no findings are pathognonomic for uveitis based on sarcoidosis Characteristic changes occur more frequently in sarcoidosis patients but none of these changes are pathognonomic for this disease

In contrast to *James* (25) who in his material mainly found anterior uveitis we found only one patient with anterior uveitis whilst the remaining 13 were panuveitis and we have not been able in our small sarcoidosis material to demonstrate two quite different syndromes as stated by him

This study will be continued partly for scientific reasons partly also to see whether the early institution of steroid treatment with sarcoidosis will prevent severe reduction in visual acuity (29) and whether it can prevent other manifestations

Abstracts

In a material of 108 patients with endogenous uveitis sarcoidosis was found to be the etiological factor in 13 % of the whole material and in more than 20 % of the bilateral cases

In 77 of these patients mediastinoscopy was performed with biopsy of the hi

lary lymph nodes and among these microscopy demonstrated in 14 cases giant cell granuloma as an expression of sarcoidosis

No serious complications followed the mediastinoscopy which was performed under general anaesthesia by the chest surgeons

X ray of the chest showed definite normal conditions in 5 of the patients in whom mediastinoscopy with biopsy demonstrated sarcoidosis

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25 *James D G et al* Ocular Sarcoidosis Brit J Ophthal *48* 461 470 1964
26 *Woods A C* Endogenous Inflammations of the Uveal Tract Baltimore Williams & Wilkins 1961
27 *James D G* Treatment of Sarcoidosis The Lancet (Sept. 9) 526 528 1967
28 *Witmer R* Klinik der Uveitis Labordiagnostik Ophthalmologica *149* 390 404 1965
29 *Bech K* Chronic Iridocyclitis An Analysis of the Occupational Prognosis in a Series of Patients from the Royal Institute for the Blind Acta Ophthal *39* 963 963 1961

Arnall Pat & Richard E Hoover Protection of Vision in Children Springfield. Charles C. Thomas 1969 Pp 17? Price 10 $

This book *is not written* for eye specialists but for pediatricians family and school physicians teachers and parents In this respect it presents valuable information about the conditions and affections commonly inducing visual defects The major project should be a visual or better eye screening in pre school age or as early as possible An interesting eye screening is the simple photographic recording of the eyes of infants with a portable camera The photographs are reviewed by an ophthalmologist in much the same way X ray films are read by radiologists The problems of oxygen for prematures and in respiratory distress are dealt with and so are genetic counseling for *eye disorders protection* against and management of eye injuries reading problems and optical aids

P Brændstrup

Biblioteca degli Annali di Ottalmologia e Clinica Oculistica Volume I Scritti in onore del Prof Luigi Maggiore Parma Maccari 1963 Pp ?03

An imposing volume honouring emeritus professor Luigi Maggiore of the university eye department in Genova Italy 41 excellent contributions

P Brændstrup

Kittel Viktor Therapeutische Empfehlungen zur Behandlung von Augenkrankheiten. 2 nd ed Leipzig V E B Georg Thieme 1969 118 pages (Abhandlungen Augenheilkunde Vol 31) Price M 14 ?0

This little book, written by Professor Kittel of the Eye Clinic, Berlin, D D R. is addressed mainly to the younger ophthalmologists A number of the therapeutic principles agree with those in use in Denmark.

In panophthalmia irrigation of the anterior chamber with antibiotics (penicillin, chloramphenicol tetracyclines erythromycin) is used

The amino acid antagonist Alnasid (fluorophenylalanine) is mentioned as a possibly *instead of 5 iodo 2 deoxy uridine in the treatment of viral disease*

Among older remedies injections of dionine and milk are still used

Temporal arteritis is treated by bilateral resection of the temporal arteries instead *of immediate steroid* medication.

Subconjunctival implantation of placental tissue in retinitis pigmentosa has been tried but without definite objective improvement.

The indications for *system c steroid* therapy and for systemic vascular dilatation appear to me to be too wide

In recurrent corneal erosion a local anaesthetic even cocaine ointment, *is recommended* although in our *opinion this* is contra indicated

Dreisler s flame sterilization of tonometers is rightly emphasized in preference to cleaning the tonometer footplate *with ether or with hydrargyrioxycyanate.*

It is interesting to observe the difference between East German and Scandinavian

23 *Bauer H* & *Lofgren S* International Study of Pulmonary Sarcoidosis in Mass Chest Radiography Acta Med Scand Suppl *425* 103 105 1964
24 *Horwit O et al* Epidemiology of Sarcoidosis in Denmark Dan Med Bull *14* 178 182 1967
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about the possibilities and advantages by this differentiated examination of the normal ocular fundus and in common and more rare affections The documentation is accompanied by many instructive coloured drawings which illustrate the varied and interesting configurations of the fundal details when observed in the differently coloured light

P Brændstrup

tradition but apart from that the book is probably not of major interest to Scandinavian ophthalmologists

M S Norn.

Walsh Frank B and Hoyt W Fletcher Clinical Neuro Ophthalmology 3rd edition Vol I II & III 2763 pages The Williams & Wilkins Co Baltimore, 1969 Price $ 120 00

Walsh s Neuro Ophthalmology has always been a voluminous book but this 3rd edition is larger than any before it having almost 3000 double columned pages This edition also has a much larger number of illustrations than the earlier ones

The first edition appeared in 1947 and was reprinted in 1948 and 1952 Then, the second edition appeared in 1957 reprinted in 1961 The third edition is no reprint or either a revised edition but has been almost completely rewritten

Of course it is a matter of judgment how much neurology and how much ophthalmology is to be included in a Neuro Ophthalmology The authors have included a great deal and that is a good thing because then we can still resort to Walsh when faced with puzzling cases in practice

Another good thing is the large number of case reports scattered in the text to illustrate so admirably and supplement the description of many of the disease conditions

The first volume in its first four chapters provides basic information pertaining to the functional anatomy of the visual oculomotor sensory and autonomic nervous systems The fifth chapter concerns the diagnosis of changes in the optic disc Chapter 6 deals with congenital anomalies and Chapter 7 with heredofamilial and degenerative diseases

In Vol II metabolic and toxic diseases muscular disorders infections parasitic invasions and vascular lesions are described

The contents of Vol III are Orbital ocular and intracranial tumours traumas ocular signs in neurasthenia hysteria and malingering This is followed by an account of neurotoxic substances affecting the visual and ocular motor systems

In such a book which is intended to serve as a manual it is of course of the utmost importance that the subject indices be as exhaustive and accurate as they are It greatly facilitates the survey that a complete subject index for all 3 volumes is printed at the end of each volume A special index of drugs and toxic substances is also given.

The references from previous editions have been supplemented by numerous modern ones

The previous editions of Walsh Neuro Ophthalmology were good too but this 3rd edition is increased and renewed Walsh has kept up to date and is still at the top as an extremely useful source of clinical ophthalmo neurological information

Holger Ehlers

А М Водовозов «Офтальмохромоскопия» *A M Vodovozov* Ophthalmochromoscopy Moscow Meditsina 1969 Pp 168 Figg 217 Price 3p 03k

This atlas written in Russian represents an introduction in ophthalmoscopy with lights of different spectral composition red yellow blue yellowish green and purple ophthalmochromoscopy After a description of the special technique follows information

ACTA OPHTHALMOLOGICA VOL. 48 1970

Aus der Universitäts Augenklinik Rostock – DDR
(Direktor Prof Dr G Pietruschka)
und der Universitäts Hals Nasen- und Ohrenklinik Rostock – DDR
(Direktor Prof Dr K Dietzel)

ZUR FRAGE DES GLEICHZEITIGEN VORKOMMENS VON GLAUKOM UND COCHLEO VESTIBULAREN STÖRUNGEN

VON

H P VICK und U VICK

Seit von *Hansen* (1880) und von *Rampoldi* (1889) auf die Beziehungen zwischen Meniere scher Erkrankung (Hansen) bzw Schwerhörigkeit (Rampoldi) und Glaukom hingewiesen wurde haben sich zahlreiche Untersucher mit dem Vergleich der Druckverhältnisse in Auge und Innenohr befasst. Dass es bis heute noch nicht zu einer Beantwortung dieser Frage gekommen ist deutet auf die Schwierigkeiten dieses Problems hin

Relativ häufig beschrieben ist das synchrone Auftreten von akuten intraokularen Drucksteigerungen bei der Meniere schen Erkrankung umgekehrt kann es beim akuten Glaukom zu Meniereähnlichen Symptomen kommen so dass gelegentlich die Bezeichnung *extraokulares Glaukomsymptom« (Tille)* gebraucht wurde.

Die anatomischen Analogien von Auge und Innenohr insbesondere das Vorhandensein eines Flüssigkeitskörpers in beiden Sinnesorganen lassen an gemeinsame ätiologische Momente bei der hydrodynamischen Dystonie als die sowohl das Glaukom wie auch die Meniere sche Erkrankung aufgefasst werden denken (Sokolowski Godfredsen Mc Grath Magdalena Castineira Ten Doesschate u a)

Nicht nur beim akuten Glaukom sondern auch bei chronischen Glaukomformen soll es nach Ansicht zahlreicher Autoren signifikant häufig zur Mitbeteiligung des stato akustischen Organes kommen Innsbesondere wird immer wie

Eingegangen am 1 Juni 1969

5th Vienna Seminar on Clinical Echoophthalmography (training program for beginners and advanced students)

Date 11 15 May 1970

Place II Ophthalmology Service (Head Prof Dr J Boeck) University of Vienna Medical School Alserstrasse 4 1090 Vienna Austria

Languages English French German

Subjects

1 Basics – physics and technology of ultrasound
2 A simple and quick method for testing system preformance
3 Optimum system settings for clinical work
4 Examination technique (echography of the eye and orbit)
5 Ultrasonic (differential) diagnosis in diseases of the eye retinal and choroid detachment choroid sarcoma metastatic carcinoma benign tumors pseudotumors retinoblastoma retrolental fibroplasia hemorrhages and other opacities of the vitreous foreign bodies etc
6 Ultrasonic (differential) diagnosis in diseases of the orbit tumors pseudotumors traumatic changes endocrine exophthalmos foreign bodies etc
7 Non traumatic tissue differentiation by ultrasound
8 Ultrasonic oculometry
9 Kretztechnik s new standardized diagnostic system (series 7200) for use in ophthalmology and tissue differentiation

For inquiries and registration
Dr Karl Ossoinig c/o II Ophthalmology Service University of Vienna Medical School
Alserstrasse 4 1090 Vienna Austria

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J H King Jr M D Director The Society of Eye Surgeons
5255 Loughborough Road N W Washington D C U S A 20016

Fruhsymptom des Glaukoms sehen So soll bei Glaukomanfallsbereitschaft der Lautheitsausgleich auftreten und in *der normotonen Periode* wieder verschwinden Diese fur die Glaukomdiagnostik sehr hoffnungsvoll klingenden Ergebnisse konnten jedoch von anderer Autoren nicht bestatigt werden und haben somit keinen Einzug in die Glaukomdiagnostik gefunden

Pietruschka schliesst aus der *audiometrischen Untersuchung* von 120 Glaukompatienten (35 Glaucoma simplex 30 Glaucoma *chronicum congestivum* 25 akute Glaukome 10 Sekundarglaukome 5 Pseudoglaukome 5 Buphthalmus Patienten) dass besonders nach dem 50 Lebensjahr haufig eine uber das altersgerechte Horen hinausgehende Innenohrschwerhorigkeit *auftritt die sich* aber nicht von der Presbyakusis abtrennen lasst und Ausdruck der bei Glaukompatienten festgestellten Haufigkeit der Arteriosklerose sein konnte Einen sicheren Zusammenhang zwischen Glaukom und Schwerhorigkeit sieht Pietruschka nicht insbesondere da sonst viel *haufiger Beziehungen zwischen dem Ausmass der* glaukomatosen Veranderungen am Auge und dem Grad der Schwerhorigkeit auffallen mussten Auch waren bei seitendifferenten Augenbefunden entsprechende Audiogramme zu erwarten Ebenso aussert sich Leydhecker zuruckhaltend *und betont dass auf Grund der vorliegenden* Untersuchungen *ein signifikantes* Zusammentreffen von Glaukom und Hypakusis als nicht gesichert angesehen werden kann. Schroder gibt zu bedenken dass das chronische Glaukom vorwiegend in hoheren Altersklassen vorkommt und dass man die Kombination Glaukom *mit Schwerhorigkeit bei Horverlust in den hohen* Frequenzen zunachst einmal auf das Alter beziehen muss Massimeo und Salonna heben hervor dass man cochleo vestibulare Storungen bei Glaukomkranken nicht in jedem Fall in ursachlichem Zusammenhang sehen sollte Die Autoren untersuchten 34 Glaukompatienten *sie fanden in 27 Fallen eine Innenohrschwerhorigkeit* im Bereich der hohen Frequenzen und zweimal eine Vestibularisstorung Da es sich jedoch durchweg um Patienten im fortgeschrittenen Alter handelte und die gefundenen Audiogramme fast ausnahmslos typischen Bildern der Altersschwerhorigkeit entsprechen warnen die Autoren *vor zu weitgehenden* Schlussen

So gehen die bisherigen Meinungen zum Problem Glaukom und Schwerhorigkeit von absoluter Bejahung uber zuruchhaltende Auffassungen bis zur Ablehnung eines Zusammenhanges weit auseinander

Untersuchungsmethode

115 in der Universitats Augenklinik Rostock stationar behandelte Glaukompatienten wurden in der *Universitats* Hals Nasen und Ohrenklinik Rostock einer eingehenden Untersuchung des Hor und Gleichgewichtsorganes unterzogen

der auf den Zusammenhang zwischen Glaukom und Innenohrschwerhörigkeit hingewiesen Lampé und Mitautoren untersuchten 33 Patienten mit primärem Glaukom und fanden bei 30 eine »Schwerhörigkeit nervalen Ursprungs« Ciurlo sah unter 15 Patienten mit Glaucoma simplex 5 mit einer hochgradigen Schwerhörigkeit die im Innenohr oder weiter zentral lokalisiert war Als Ursache nimmt der Autor gefässneurotische Störungen vermutlich durch Schädigung des Sympathicus an Beretta et al kommen nach Untersuchung von 42 Patienten mit Glaucoma chronicum und 2 Fällen von akutem Glaukom zu dem Schluss dass insbesondere beim chronischen Glaukom ein pathogenetischer Zusammenhang zwischen Glaukom und Schwerhörigkeit sehr nahe liegt wobei gleichzeitige neurovegetative Störungen der Kapillardurchlässigkeit sowohl im Innenohr als auch in der Uvealmenbran des Auges ursächlich erwogen werden

Sokolowski registrierte bei 40 Glaukomkranken in 58 % eine Hypakusis. Bietti und Porta konnten bei Glaukompatienten bei Flüssigkeitsbelastungsproben eine Parallelität zwischen der Zunahme des intraokularen Druckes und der audiometrisch nachweisbaren Hörminderung feststellen Bei Augengesunden blieb das Audiogramm bei Flüssigkeitsbelastungen unbeeinflusst (Bietti) Ten Doesschate audiometrierte 26 Glaukompatienten und kam zu dem Ergebnis dass denselben eine Perzeptionsschwerhörigkeit gemeinsam ist die in ihrem Ausmass Beziehungen zum intraokularen Druck weniger zur Einschränkung des Gesichtsfeldes aufweist Czaplicka und Mitarbeiter stellten bei 27 Untersuchten mit Glaucoma simplex in 66 % eine Perzeptionsschwerhörigkeit fest Die Autoren sahen in dem hohen Prozentsatz den Beweis für einen ursächlichen Zusammenhang zwischen beiden Krankheiten Eine Abhängigkeit zwischen dem Grad der Augenerkrankung und dem Funktionsverlust des Innenohres war nicht erkennbar

Gartner gelangte durch das von ihm beobachtete gehäufte Auftreten von Innenohrschwerhörigkeit beim Pigmentglaukom zu der Auffassung dass in diesen Fällen möglicherweise ein Zusammenhang der Pigmentstörung im Auge mit einer entsprechenden Störung des Innenohrpigments vorliegt Bei 6 Patienten mit Pigmentglaukom hatte der Autor in 4 Fällen eine ungeklärte Innenohrschwerhörigkeit gefunden Diese Ansicht wurde Unterstützung finden durch die Beobachtung von Innenohrschwerhörigkeit bei sympathischer Ophthalmie Vogt Koyanagi – Syndrom und Haradascher Erkrankung Auch hier wurde auf eine komplexe Störung des Pigmentes hingewiesen (Hager Peters) Kramer et al nehmen auf Grund ihrer Untersuchungen an dass ein ursächlicher Zusammenhang zwischen Glaukom und Innenohrschwerhörigkeit besteht Von 124 Glaukompatienten wiesen 42 eine über das altersphysiologische Mass hinausgehende Perzeptionsschwerhörigkeit auf vorwiegend vom cochleo basalen Typ wie sie auch bei der Presbyakusis gefunden wird Chilaris et al wie auch Ferraris de Gaspare und Mitarbeiter gehen sogar so weit dass sie im Verhalten des charakteristischen Audiogramms und im Auftreten des Recruitmentphänomens ein

Tɩbelle II

Cegenuberstellung vɩn Glaukomtyɩ zu n H rvern ogen der Claukompatienten

	Claucoma simplex	Chron kong Glaukom	Akutes Glaukom	I igment glaukom	Juveniles Glaukom	Buphthalmus	Summe
N rmalh ıren le	38	8	–	4	3	1	54
Altersgerecl tes H rverm gen	17	4	–	3	–	–	24
Innen ıhrschwerh ɪrigkeit mit geklarter Ätiologie	1	3	1	–	–	–	19
Innenc hrschwerhorigkeit unklarer Genese	15	1	1	–	1	–	18
	85	16	2	7	4	1	115

Tabelle I

Die 115 untersuchten Glaukompatienten liessen sich nach Glaukomtyp Geschlecht und Durchschnittsalter aufgliedern

Glaukomart	Anzahl	Geschlecht ♂	♀	Durchschnittsalter
Glaucoma simplex	85	38	47	53 4
Glaucoma chronicum congestivum	16	9	7	56 4
Akutes Glaukom	2		2	63 5
Pigmentglaukom	7	5	2	56 6
Juveniles Glaukom	4	4		2[illegible] 8
Buphthalmus	1	1		12 0
Summe	115	57	58	47 8

Bei der Erhebung der Anamnese wurde besonders auf durchgemachte Infektionen und Intoxikationen chronische und akute Lärmtraumen sowie Stoffwechselerkrankungen Wirbelsaulenerkrankungen und Schädelunfalle geachtet Nach der audiometrischen (Schwellenaudiogramm Geräuschaudiogramm nach Langenbeck) und röntgenologischen (nach Stenvers bzw Pyramidenvergleichsaufnahmen) Untersuchung erfolgte die Prüfung des Vestibularorgans (Schwindelanamnese Prufung des Lage und Lagerungsnystagmus sowie thermische Reizung)

Untersuchungsergebnisse

Die audiometrische Untersuchung ergab bei 54 (47 0 %) der 115 Patienten ein normales Horvermogen mit einem Kurvenverlauf des Audiogramms fur Luft- und Knochenleitung zwischen 0 und 10 dB Von den verbleibenden 61 Patienten (53 0 %) zeigten 24 einen rein altersbedingten Gehornachlass wobei die diesbezugliche Bewertung nach den von Jatho und Heck angegebenen Horkurven erfolgte

37 Probanden wiesen also eine uber das ihrem Alter entsprechende physiologische Mass hinausgehende Schwerhorigkeit auf Von dieser Gruppe mussten jedoch bei kritischer Auswertung 19 Patienten abgesondert werden auf Grund langjahriger Lärmexposition akuter Larmtraumen und Schadelverletzungen sowie Schalleitungsschwerhorigkeiten Zu dieser Gruppe gehorten auch 3 Patienten mit einer kombinierten Schwerhorigkeit bei denen man eine toxische Genese des Innenohrschadens annehmen musste

Tabelle II

Gegenüberstellung von Glaukomtyp zum Hörvermögen der Glaukompatienten

	Glaucoma simplex	Chron. kong. Glaukom	Akutes Glaukom	Pigmentglaukom	Juveniles Glaukom	Buphthalmus	Summe
Normalhörende	38	8	–	4	3	1	54
Altersgerechtes Hörvermögen	17	4	–	3	–	–	24
Innenohrschwerhörigkeit mit geklärter Ätiologie	15	3	1	–	–	–	19
Innenohrschwerhörigkeit unklarer Genese	15	1	1	–	1	–	18
	85	16	2	7	4	1	115

Es blieben 18 (15 8 %) Patienten mit einer uber das altersphysiologische Mass hinausgehenden Innenohrschwerhörigkeit die auch bei sehr kritischer Bewertung der Anamnese und des objektiven Ohrbefundes zunächst atiologisch nicht zu klären war Bei diesen Probanden ist ein Zusammenhang zwischen dem Glaukom und der Innenohrschwerhorigkeit zu diskutieren Einschrankend muss jedoch schon hier gesagt werden, dass es sich bei einem Teil der Falle nur um gering uber das altersphysiologische Mass hinausgehende Perzeptionsschwerhorigkeiten handelt

Um die Lokalisation des Hörschadens im Labyrinth bei den 18 atiologisch unklaren Hörminderungen naher zu bestimmen wurden die Audiogramme nach Langenbeck in vier Haupttypen eingeteilt Dabei zeigte sich dass in uberwiegender Anzahl (13 von 18) der Kurventyp A (cochleo basaler Typ) auftrat wie er bevorzugt fur die Altersdegeneration des Hororgans typisch ist (Tab III) Dieses Ergebnis unterstutzt die von Pietruschka geausserte Meinung dass es auf Grund einer verstärkten Arteriosklerose bei Glaukompatienten zu einer uber das Alter hinausgehenden Presbyakusis kommen kann

Unter den 18 Patienten mit den atiologisch unklaren Innenohrschwerhorigkeiten ergaben sich bei 8 Kranken seitendifferente Audiogramme wobei jedoch nur einmal eine Übereinstimmung mit einem entsprechenden seitendifferenten Augenbefund bestand

Bei der Gegenuberstellung der Audiogramme und der augenarztlichen Befunde konnte keine Abhangigkeit des Horbefundes zur Glaukomdauer zum Visus und Gesichtsfeldverfall sowie zum Grad der glaukomatosen Exkavation der Papillen gefunden werden Ebenfalls ergaben sich keine Beziehungen zwischen der Hohe des intraokularen Druckes der Weite des Kammerwinkels der eingeschlagenen medikamentosen oder operativen Druckregulierung und dem Horkurvenverlauf So wurde z B bei beiden Patienten mit akutem Glaukom

Tabelle III

	Glaucoma simplex	Chron kong Glaukom	Akutes Glaukom	Juveniles Glaukom	Summe
A Corti Typ	9	1	1	1	13
C Corti Typ	1	–	–	–	1
A Corti/Nerv Typ	1	–	–	–	1
C Corti/Nerv Typ	1	–	–	–	1
A/C Typ	2	–	–	–	2
B/C Typ	1	–	–	–	1
	15	1	1	1	18

im Anfall ein Audiogramm am Krankenbett geschrieben *und es zeigten sich* nach erfolgter *Drucksenkung* (einmal medikamentös einmal operativ) bei einem *Kontrollaudiogramm* keinerlei Differenzen im Kurvenverlauf

Diese Ergebnisse decken sich mit den Aussagen von Pietruschka Kramer et al Czaplicka et al Lampe et al. und stehen *im Gegensatz zu* den Befunden von Tillé Ten Doesschate et al und Bietti c. s die Zusammenhänge zwischen der Höhe des intraokularen Druckes bzw der Dauer des Glaukoms und dem Grad der Innenohrschwerhörigkeit sahen

Bei der Prüfung des *Vestibularorgans fand sich* unter den 115 Glaukompatienten nur in 2 Fällen eine Untererregbarkeit bei der kalorischen Reizung Ein Patient wies einen horizontalen mittelfrequenten mittelamplitudigen Spontannystagmus auf und bei einem weiteren Patienten bestand eine *einseitige Untererregbarkeit* bei normaler Erregbarkeit des anderen Labyrinths 14 Untersuchte klagten bei der anamnestischen Befragung über Schwindel Bei allen Patienten ergab sich keine Korrelation zum Augen und Hörbefund

Zusammenfassung

Um einen in der Literatur wiederholt beschriebenen Zusammenhang zwischen dem funktionellen und organischen Befund beim primären Glaukom und entsprechenden Hörstörungen am Innenohr nachzuprüfen wurden bei 115 Glau*komkranken eingehende Untersuchungen des Hör ud Gleichgewichtsorganes* durchgeführt Auf Grund der mitgeteilten Untersuchungsergebnisse scheint kritische Zurückhaltung bei der Beurteilung des Zusammenhanges zwischen Glaukom und Innenohrschwerhörigkeit geboten

In untersuchen Beobachtungsgut steht den 18 Patienten mit einer ätiologisch unklaren Innenohrschwerhörigkeit eine Gruppe von 97 Glaukompatienten mit normalem bzw altersentsprechendem Hörvermögen oder eindeutig anamnestisch erklarbarer Schwerhörigkeit gegenüber

Ein gemeinsamer Faktor der beiden Erkrankungen in signifikanter Häufigkeit zu Grunde liegen konnte konnte nicht aufgedeckt werden Bei der Auswertung der Geräuschaudiogramme nach Langenbeck fand sich überwiegend der Cochleo basale Typ (Typ A) der charakteristisch bei altersdegenerativen Prozessen häufiger vorkommt

Wenn die relativ geringe Anzahl von Schwerhörigkeiten unter unseren untersuchten Glaukompatienten in einem gewissen Widerspruch zu *Ergebnissen* anderer Untersucher steht so ist dies möglicherweise mit dem bewusst niedrig gehaltenen Durchschnittsalter *unserer Probanden* zu erklären.

Zwischen dem Grad der glaukomatösen *Veränderungen* und den Hörkurven sowie den Vestibularisbefunden bestanden keine Beziehungen

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THE OCULAR PULSE – TECHNICAL FEATURES

BY

MILTON BEST M D THOMAS A KELLY M S
and MILES A GALIN M D

Ocular techniques to study carotid occlusive disease include ophthalmodynamometry carotid compression tonography and ocular pulse measurements Studies using this latter method have been concerned primarily with the amplitude of the recorded pulse and it has been noted that a reduction in amplitude of the ocular pulse occurs on the side of carotid occlusive disease (*Castren et al* 1964 *Bynke* 1966 1968a 1968b and 1969 *Bynke and Krakau* 1964 *Lester* 1966 *Bron et al* 1967 *Galin et al* 1967b) Changes in the contour of the ocular pulse recordings have not received much attention although contour analysis has been of great importance in peripheral vascular disease (*Winsor* 1959)

Ocular pulses recorded from the surface of the eye with a suction cup are similar in all respects to pulses recorded by direct cannulation and reflect the pressure changes occurring in the eye during the cardiac cycle (*Lawrence et al* 1966) This report concerns itself with a consideration of the suction technique used to record ocular pulses and the effects of various physical factors upon the pulse amplitude peak characteristics and notching

Methods

The technique utilizes a a dome shaped aluminum or plastic suction cup with an outside diameter of 14 mm and an inside diameter of 12 *presently* employed

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in suction ophthalmodynamometry (*Galin et al* 1969a and 1969b) In patients it is placed in contact with the conjunctiva adjacent to the temporal limbus while in rabbits or other experimental animals it is placed directly on the cornea The suction cup is attached to a P23BB Statham transducer by polyethylene tubing (PE 190) with a three way stopcock between the transducer and the suction cup (figure 1) Polyethylene tubing (PE 190) leads from the second arm of the transducer through a three way stopcock to a column of saline that is below the level of the transducer and can provide variable amounts of suction. The entire system is filled with saline All tubes must be free of small air bubbles

The pulses are recorded from both eyes simultaneously on a Beckman type R dynograph with a type 9803 strain gauge coupler and a type 482 dynograph amplifier The transducers are first opened to air and balanced at a sensitivity setting of 0 5 millivolts per centimeter so that a 1 cm deflection equals 2 mm Hg The sensitivity setting on both channels is then increased to 0 05 or 0 1 millivolts per cm and the polarity switched to negative The zero setting is adjusted until a pulse recording appears and is centered on each channel Pulses are recorded at a paper speed of 25 mm per second

In all experiments rabbits weighing between 3 and 4 kg were anesthetized with intravenous pentobarbital 25 to 37 5 mg Proparacaine hydrochloride was used topically Intraocular pressure was controlled with a saline reservoir through a 23 gauge needle inserted into the anterior chamber Either an open or closed manometric system was used and intraocular pressure was continu

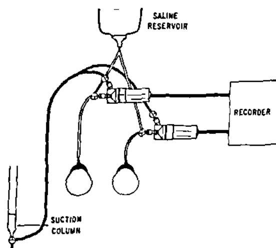


Fig 1
Schematic representation of apparatus to record ocular pulses

ously recorded through a three way stopcock using a P23BB Statham trans ducer

The suction cup was applied to the cornea while saline was flowing freely through it from a reservoir When all air bubbles were eliminated from the cup it was firmly applied to the globe and the stopcock was turned to disengage the reservoir and connect the cup to the suction column.

The relationship between intraocular pressure before and after suction equi valent to -40 cm saline was applied is shown in figure 2 where intraocular pressure was varied from 5 to 75 mm Hg using a closed manometric system prior to application of the suction cup

Analysis of Factors

1 The Amount of Suction Figure 3 illustrates the effect of various amounts of suction on the intraocular pressure when a closed manometric system was used to establish an initial intraocular pressure of 21 mm Hg A linear relationship exists between the level of suction and the subsequent increase of intraocular pressure in the range studied The highest pressure reached was 46 mm Hg with suction equivalent to -50 cm saline. The amplitude of the ocular pulse bore a similar linear relationship to the level of suction (figure 4) Figures 3 and 4 are plotted from recordings obtained from the same eye and are repre sentative of a series of six eyes

In order to eliminate the effect of the suction induced increase in intraocular pressure on the amplitude of the recorded pulse, the same experiment was re peated using an open manometric system at intraocular pressures of 21 and 30

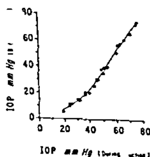


Fig 2
Relationship between intraocular pressures before and after application of the suction cup at -40 cm saline.

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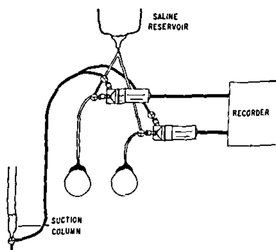


Fig 1
Schematic representation of apparatus to record ocular pulses

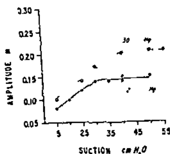


Fig 5
Effect of suction on amplitude of ocular pulse using an open manometric system at 21 and 30 mm Hg



Fig 6
Suction equivalent to ~ 0 cm saline resulted in variable pulses with double peaks Intraocular pressure was 30 mm Hg (open manometric system)

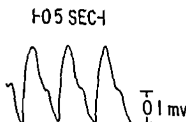


Fig 7
Suction equivalent to −40 cm saline resulted in uniform pulses with single peaks Intraocular pressure was 30 mm Hg (open manometric system)

varying the height of the saline reservoir Ocular pulses were recorded in sequences of increasing and decreasing intraocular pressures using either an open or a closed manometric system

In a second group of rabbits serial records of the ocular pulse were obtained

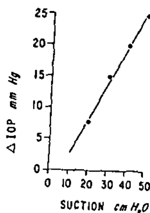


Fig 3

Effect of suction on intraocular pressure Intraocular pressure before suction was 21 mm Hg

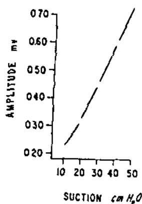


Fig 4

Effect of suction on amplitude of ocular pulse Intraocular pressure before suction was 21 mm Hg

mm Hg The results are shown in figure 5 which indicates that the maximum amplitude of the recorded pulse is obtained at suction levels between –30 and –40 cm saline in an open system

With an open or closed manometric system suction levels below –30 cm saline resulted in double peaking and variability of the ocular pulse (figure 6) At suction levels of –40 cm saline or higher the pulses were uniform and had single peaks (figure 7)

2 The Level of Intraocular Pressure While suction was maintained constant at –40 cm saline intraocular pressure was varied by two techniques In one group of rabbits different levels of intraocular pressure were obtained by

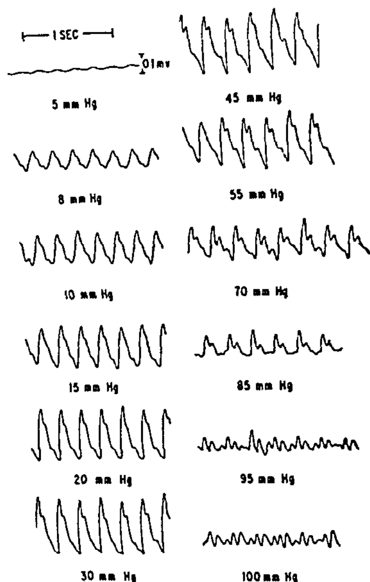


Fig 8

Effect of intraocular pressure on the amplitude and contour of the ocular pulse. Intra ocular pressure was established with an open manometric system Suction was −40 cm saline

Loosening the conjunctiva or removing it under the suction cup when it was placed eccentrically had no significant effect on the contour or the amplitude of the recorded pulse.

during the period of intraocular pressure recovery after prolonged tonometry or massage Serial measurements of intraocular pressure were made with a Schiotz tonometer and none of the eyes was cannulated while the pulses were being recorded with the suction cup

The amplitude and contour of the ocular pulse recorded with the suction cup vary with the level of intraocular pressure whether an open or closed manometric system is used to change intraocular pressure Figure 8 illustrates the changing form and amplitude of the recorded ocular pulse as intraocular pressure is elevated from 5 to 100 mm Hg in an open manometric system Notching of the descending limb of the pulse wave was more prominent at high levels of intraocular pressure than at low ones

The level of intraocular pressure at which the maximum amplitude of ocular pulsation in recorded in a closed manometric system is indicated in figure 9 The two curves represent the minimum (45 mm Hg) and the maximum (55 mm Hg) intraocular pressure at which the ocular pulse of greatest amplitude was recorded in a series of six rabbit eyes All six curves had the same form and it made no difference whether the measurements were made in an increasing or decreasing sequence of intraocular pressure

With the open perfusion system the curves relating intraocular pressure and amplitude of the ocular pulse were affected by the sequence in which intraocular pressure was varied Figure 10 illustrates the results from an eye when the intraocular pressure was first increased and then decreased stepwise between 5 and 105 mm Hg When intraocular pressure is increased stepwise the curve forms a peak but when measurements are made as intraocular pressure is decreased stepwise there is a distinct flattening of the curve so that the maximum amplitude of the pulse wave is represented by a plateau between 30 and 60 mm Hg

There is no relationship between the amplitude of the ocular pulse and the level of intraocular pressure when intraocular pressure is lowered by prolonged tonography or massage and the ocular pulse recorded with the suction cup during the recovery period Figure 11 shows that as the intraocular pressure increases from 3 to 17 mm Hg during the recovery period after prolonged tonometry the amplitude of the ocular pulse remains essentially unchanged A similar situation exists for intraocular pressures between 6 and 19 mm Hg in the recovery period after massage This may be due to the relatively small changes in intraocular pressure that occur during the recovery period

3 Site of Application of the Suction Cup The amplitude of the ocular pulse was not altered significantly by placing the suction cup on the cornea or sclera alone or straddling both However the contour of the recorded pulse was affected in about half the rabbits tested The major effect was an accentuation of the notch on the descending limb of the pulse wave as the suction cup was moved from the central cornea toward the sclera

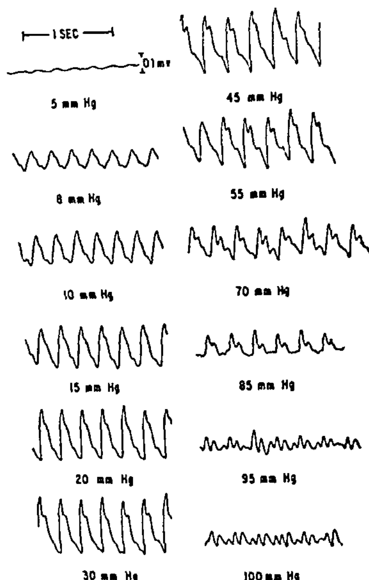


Fig 8

Effect of intraocular pressure on the amplitude and contour of the ocular pulse. Intraocular pressure was established with an open manometric system. Suction was −40 cm saline

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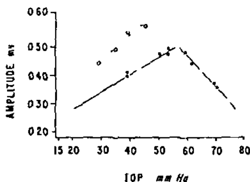


Fig 9

Relationship between amplitude of ocular pulse and intraocular pressure in two eyes Intraocular pressure was varied with a closed manometric system Maximum amplitude occurred at an intraocular pressure of 45 mm Hg (interrupted line) in one eye and 55 mm Hg (solid line) in the second eye

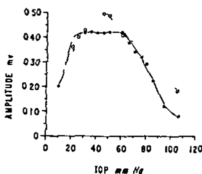


Fig 10

Relationship between amplitude of ocular pulse and intraocular pressure in one representive eye Intraocular pressure was first increased stepwise (interrupted line) and then decreased stepwise (solid line) between 5 and 105 mm Hg with an open manometric system

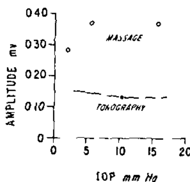


Fig 11

Relationship between amplitude of ocular pulse and intraocular pressure during the recovery period following prolonged tonography (solid line) or massage (interrupted line)

Discussion

Any technique that is used to record ocular *pulsation* should be easy to perform rapid and of sufficient sensitivity and reliability to give constant and analyzable results The suction cup technique meets these criteria The analysis of the results depends upon knowledge of the various factors that can affect the amplitude and contour of the recorded pulse

The effect of intraocular pressure on the pulse depends upon the methods which are used to vary the level of intraocular pressure and to record the pulse By recording the pulse through a cannula in the anterior chamber or vitreous Lawrence and Schlegel obtained a variety of curves relating pulse amplitude and intraocular pre sure the most common showing a plateau representing the maximum amplitude at intraocular pressures between 40 and 80 mm Hg (*Lawrence et al* 1966) When the procedure was repeated on the same eye the curve no longer had a plateau but formed a peak instead at an intraocular pressure of about 60 mm Hg and they felt this reflected a change in the physical characteristics of the intraocular blood vessels presumably an increase in blood vessel compliance

If as in this study a suction cup is used to record the ocular pulse and an *open perfusion system is used to vary the intraocular presure* the initial curves obtained all peak A plateau occurs only when amplitude is measured as intraocular pressure is lowered from its elevated starting point Although an open manometric system damps the amplitude of the recorded ocular pulse it is noteworthy that subjecting the eye to an elevated intraocular pressure with an *open system consistently alters the shape of the curve relating intraocular pressure* and pulse amplitude recorded with the suction cup in a manner exactly opposite to the curve obtained by direct cannulation experiments The explanation for this may be that there is a marked increase in ocular rigidity at all levels of intraocular pressure after the eye has been stretched by a high intraocular pressure (*Ridley* 1930) *This would result in a greater amplitude* of the ocular pulse as measured by direct cannulation since this technique measures the true pressure pulse The amplitude of the ocular pulse as measured with a suction cup however would be decreased since this technique measures movements of *the cornea* into and out of the suction cup (*Su uki* 1962)

In the non cannulated eye the emplitude as well as the contour of the suction recorded ocular pulse is not affected by lowering the intraocular pressure by tonography or massage until the intraocular pressure reaches levels of 4 to 6 *mm Hg or less* This means that during the procedure for recording ocular pulses the massage effect of the suction cup will have no effect on the amplitude or contour of *the recorded pulse unless* the procedure is unduly prolonged On the other hand elevating the intraocular pressure above normal levels has

a similar effect on the suction recorded ocular pulse in a cannulated or non cannulated eye

The effect of variations of the amount of suction on the contour of the re corded pulse is very important Below suction levels of -30 cm saline the recorded pulse wave contains numerous notches on both the ascending and descending limbs with many double peaks In addition there is extreme varia bility in both the amplitude and contour of the ocular pulse as recorded from a single eye These findings occur in both open and closed manometric systems indicating that the variability is not associated with changes in intraocular pres sure At levels of suction greater than -30 cm saline the recorded pulses are simpler in form with a definable peak and one or two notches usually limited to the descending limb Also the amplitude and contour of the recorded pulses are consistent A level of -40 or -50 cm saline is sufficient to produce a con sistent recording of the ocular pulse which can be studied with relative ease

One of the most common causes of variation in the contour of the ocular pulse is a change in the position of the suction cup The simplest technique in rabbits is to place the cup centrally on the cornea If the cup is moved toward the lim bus no alteration in the recorded pulse occurs until the edge of the cup straddles the limbus At this point there will often be an accentuation of the notch that appears on the descending limb of the pulse wave This effect usually dis appears when the suction cup is placed entirely on the sclera Looseness of the conjunctiva appears to have no effect on the amplitude or contour of the re corded pulse

In the non cannulated eye of the rabbit the ascending limb of the suction recorded pulse wave is usually free of notches or deflections whereas the de scending limb usually has a well defined notch or deflection Using an open manometric system this study shows that at intraocular pressures below 30 mm Hg and at intraocular pressures 50 mm Hg or higher the notch on the descend ing limb is absent or not prominent Changes in notching or deflection may be of importance in occlusive vascular disease Therefore -40 cm saline was chosen as the appropriate suction level for studying induced carotid lesions in rabbits since it resulted in intraocular pressures between 35 and 40 mm Hg in most animals At this level of suction slippage of the suction cup from the center of the cornea was minimal

The apparatus and technique described in this study have been used on many human subjects (*Galin et al* 1967a) Consistent ocular pulses can be recorded rapidly with a minimum of discomfort to the patient In addition this technique does not have the disadvantage of displacing the globe posteriorly into the orbit that has been described with other instruments (*Bynke* 1968c)

Summary

A technique is described for recording ocular pulses using a suction cup The contour and amplitude of the recorded pulse are affected by the amount of suction the level of intraocular pressure and the site of application of the suction cup The most easily analyzed and consistent pulses are obtained with suction equivalent to –40 cm saline which induces an intraocular pressure between 35 and 40 mm Hg Criteria of importance in analysis of ocular pulse waves include amplitude notching on the ascending and descending limbs and peak characteristics The apparatus and technique described result in consistent ocular pulse recordings that can easily be analyzed for the above characteristics

Acknowledgment

Photographs were supplied by Mr Morris Moritz Bird S Coler Hospital

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ACTA OPHTHALMOLOGICA VOL 48 1970

Aus der Universitats Augenklinik Jena
(Direktor Prof Dr A Heydenreich)

PIGMENTGESCHWÜLSTE DER BINDEHAUT

Nebst kritischer Bemerkungen zur Rontgenbestrahlung

VON

A HEYDENREICH

Pigmentgeschwulste gehoren zu den besonders malignen Tumoren und verdienen deshalb gesteigerte Aufmerksamkeit Im Bereich des Auges begegnen wir ihnen besonders in der Uvea aber auch im ausseren Teil des Auges vor allem in der Conjunktiva Die Prognose der Uveamelanome wird dabei im allgemeinen wesentlich gunstiger eingeschatzt als die der Haut und Schleimhautmelanome (*Wright* 1949)

Wahrend jedoch die Uveamelanome meist erst in fortgeschrittenem Stadium diagnostiziert werden wenn Sehstorungen auftreten oder sie rein zufallig bei einer routinemassigen Ophthalmoskopie erkannt werden sind die Bindehautpigmenttumoren dem Blick sofort zuganglich und fuhren den Patienten schon aus kosmetischen Grunden fruhzeitig zum Arzt Sie erfordern in jedem einzelnen Fall grundliche Überlegung des notwendigen therapeutischen Vorgehens und Handelns besonders da sie in vielen Fallen zunachst jahrelang als sehr gutartig erscheinen und nur gelegentlich zum Teil aus unbekannten Grunden maligne entarten

Nach *Thiel* (1965) konnen wir drei Arten von Pigmenttumoren bzw anomalien im Bereich der Konjunktiva unterscheiden

1 Die *Melanosis* Sie beginnt klinisch als kleiner flacher Pigmentfleck mit feiner granularer Pigmentation die sich allmahlich uber die ganze bulbare und palpebrale Konjunktiva die Karunkel die Hornhaut und Lider ausbreiten kann Gegebenenfalls findet man auch eine Melanosis im Inneren des Auges (Iris

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Während jedoch die Uveamelanome meist erst in fortgeschrittenem Stadium diagnostiziert werden, wenn Sehstörungen auftreten oder sie rein zufällig bei einer routinemässigen Ophthalmoskopie erkannt werden, sind die Bindehautpigmenttumoren dem Blick sofort zugänglich und führen den Patienten schon aus kosmetischen Gründen frühzeitig zum Arzt. Sie erfordern in jedem einzelnen Fall gründliche Überlegung des notwendigen therapeutischen Vorgehens und Handelns, besonders da sie in vielen Fällen zunächst jahrelang als sehr gutartig erscheinen und nur gelegentlich, zum Teil aus unbekannten Gründen, maligne entarten.

Nach *Thiel* (1963) können wir drei Arten von Pigmenttumoren bzw. -anomalien im Bereich der Konjunktiva unterscheiden:

1. Die *Melanosis*. Sie beginnt klinisch als kleiner flacher Pigmentfleck mit feiner granulärer Pigmentation, die sich allmählich über die ganze bulbäre und palpebrale Konjunktiva, die Karunkel, die Hornhaut und Lider ausbreiten kann. Gegebenenfalls findet man auch eine Melanosis im Inneren des Auges (Iris

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Aderhaut) Histologisch gleich das Bild zunächst der einfachen Pigmenthyper trophie (s u) spater findet man proliferierende pigmentierte Zellen sub und intraepithelial mit entzundlichen Reaktionen an den Wucherungsgrenzen

2 *Naevus pigmentosus* Er tritt klinisch als leicht erhabenes Gebilde in der Konjunktiva auf und enthalt meistens reichlich Pigment Histologisch findet mand die typischen Naevuszellnester mit epithelahnlichen Zellen und blaschen formigen Kernen Die Naevuszellen sind meist pigmentarm die daruberliegende Epidermis und das umgebende Bindegewebe stark pigmentiert Nach Albertini handelt es sich um eine "dysontogenetische Geschwulst im Sinne eines Hamar toms Sie konnen angeboren oder erworben sein und entstehen meist im ersten Dezenium

3 *Melanom* die eindeutig bosartige Geschwulst Sie ist klinisch durch rasches Wachstum Prominenz und Gefassreichtum und histologisch durch karzinoma tösen oder sarkomatosen Zellaufbau gekennzeichnet Im allgemeinen entwickelt sie sich erst im 4 und 5 Lebensjahrzehnt

Als 4 Gruppe wird vielfach das juvenile Melanom (*Spitz* 1948) abge grenzt das sich klinisch durch einen gutartigen Verlauf auszeichnet histolo gisch jedoch als auffallend maligne erscheint Eine Differenzierung vom malig nen Melanom ist auf Grund mehrkerniger Riesenzellen die dem Toutontyp ah neln, gewisser Einformigkeit und mangelndem Pleomorphismus der Zellen fast volligem Fehlen von Pigment und naevuszellartigen Strukturen moglich Es wird nicht nur im Kindesalter sondern in etwa 15 % der Falle auch bei Er wachsenen beobachtet (*Allen* 1960) Thiel hält eine strenge Abgrenzung des juvenilen Melanoms von den Pigmentzellnaevi fur nicht berechtigt Infolge des geringen Pigmentgehaltes ist klinisch eine Verwechslung mit Angiomen tele angiektatischen Granulomen möglich

Schliesslich muss man von diesen 4 Gruppen noch die einfache *Pigmenthy pertrophie* abtrennen die gelegentlich auch an eine maligne Pigmententartung denken lassen kann besonders wenn es zu einer – auch für den Patienten auf fallenden und zunehmenden Pigmentierung im Bindehautbereich kommt wie z B bei Pat Erika St 14 J 1963

Anamnese Seit 12 Jahren von den Eltern im rechten Auge ein Muttermal beob achtet, das grosser geworden sei Seit 2 Jahren auch am linken Auge ein Muttermal beobachtet

Befund Beiderseits befindet sich nasal in Nahe des Limbus in der Conjunctiva bulbi eine Pigmentansammlung (Abb 1) An der Spaltlampe erkennt man zusatzlich zahl reiche Pigmentzellen fast zirkular am Limbus Exzision des Pigmentfleckes rechts

Histologisch Bindehautstuck mit stark pigmentierten Zellen im basalen Anteil der Epithelschicht Einzelne Chromatophoren im subepithelialen Gewebe keine Naevus zellen (Abb 2) Befund 23 6 1966 Rechts zarte Bindehautnarbe mit einzelnen Pig mentkornchen Links unveranderter Pigmentfleck

Die einfache Pigmenthypertrophie stellt eine vermehrte Ansammlung von Pigmentzellen dar die normalerweise am Limbus corneae und gelegentlich



Abb 1
Pigmenthypertrophie am rechten Auge (Pat Erika St)



Abb 2
Histologischer Befund von Abb 1 H E Farbung

auch in der angrenzenden Conjunctiva bulbi bei allen pigmentierten Tier und Menschenrassen and *in etwa 2/3 der Falle auch in geringem* Umfange bei der mitteleuropaischen Bevolkerung vorkommen und in bestimmten Lebensphasen (Pubertat Graviditat) eine Vermehrung bzw Hyperpigmentation zeigen konnen. Histologisch handelt es sich vor allem um Pigmentzellen epithelialen Typs in der Basalschicht des Epithels und um einzelne Chromatophoren im mesenchy malen subepithelialen Gewebe Sie werden auch in ihren Vorstufen (Propig ment) besonders gut mit der Methode nach Masson Hamperl dargestellt (s auch *Heydenreich* 1968)

Pigmentnaevi und Melanosis konnen sich vergrossern und den Eindruck des bosartigen Wachstums hervorrufen ohne dass histologisch schon eine Maligni

tät nachzuweisen ist Es handelt sich dabei um Einlagerung von Pigment in die Umgebung und nicht um Destruktion des benachbarten Gewebes Eine maligne Entartung ist aber durchaus möglich wobei klinisch eine Zunahme der Pigmentierung höckrige Gewebswucherung Gefässreichtum und Hyperämie (Abb 3) und nach Thiel eine Trubungszone in der angrenzenden Hornhaut ahnlich dem Arcus lipoides hinweisend sind Histologisch fällt eine erhebliche Wucherung Entdifferenzierung der Grundelemente mit abnormer Zellgrosse Vakuolenbildung Kernvermehrung und -atypien und destruktive invasive Proliferation auf So gibt es für das Zustandekommen eines Melanoms drei Moglichkeiten Entartung einer Melanosis Entartung eines Pigment Naevus und Entstehung einer primären malignen Pigmentgeschwulst auf vorher unveränderter Haut bzw Bindehaut Als Urche der Entartung werden vielfach geringfugige Traumatisierungen (auch Probeexzisionen!) oder entzundliche Veranderungen (akuter heftiger Bindehautkatarrh) angenommen Endokrine Faktoren (Pubertät Schwangerschaft ACTH Behandlung) können als Wachstumsreiz wirken (*Cook* 1952 *Thiel* 1965) Haufig fehlen jedoch aussere Anhaltspunkte so dass Thiel u a die Entstehung aus primär vorhandenen atypischen Melanozysten annehmen

Die langere Beobachtung mehrerer pigmentierter Bindehauttumoren mag auf die Problematik der klinischen und histologischen Diagnostik und der daraus abgeleiteten Therapie hinweisen (s auch *Lapp* 1969)

Bei einem stationaren augenärztlichen Krankengut von 12 526 Patienten



Abb 3

Pigmentzellnaevus am linken Auge (Fall 2 Tab 1)

(1955 1965) fanden sich 440 Tumorträger davon hatten 24 Patienten Tumoren der Bindehaut und Karunkel bei 12 dieser Patienten handelte es sich um Pigmenttumoren 8 Naevi pigmentosi und 4 Melanome (s Tab 1 und 2)

Die 8 *Pigmentnaevi* bestanden aus 2 5 mm grossen meist stark pigmentierten leicht erhabenen Knoten die in Nahe des Limbus bzw der Karunkel sassen Haufig waren *die umgebenden Gefasse erweitert* Bei 3 Fallen tauchte klinisch der Verdacht eines malignen Melanoms auf besonders da bei Fall Nr 1 ein starkeres Umgebungsodem bestand bei Fall Nr 4 wahrend einer Graviditat die Pigmentierung stark zunahm und bei Fall Nr 5 die Geschwulst relativ gross (5 mm) und stark durchblutet war Auch histologisch bestand Melanomverdacht Das Alter der Patienten lag zwischen 5 und 32 Jahren die Tumoren wurden von den Patienten meistens erst seit 1/2 1 Jahr gelegentlich schon seit 3 4 Jahren bemerkt Die Therapie bestand in allen Fallen in einfacher chirurgischer Exstirpation bei Fall 5 und 6 in einer *zusatzlichen Rontgenvorbestrahlung* (5400 8000 R) Ein Rezidiv bzw maligne Entartung wurden in der Nachbeobachtungszeit von 3 10 Jahren nicht festgestellt

Die 4 *malignen Melanome* zeigten demgegenuber ein ganz anderes Verhalten So konnte die Diagnose einer Malignitat anhand des progressiven Wachstums *der Grosse des tumorosen Prozesses und des Gefassreichtums schon* klinisch eindeutig gestellt werden In 2 Fallen (Nr 3 und 4) war auch die von Thiel beschriebene randnahe Hornhauttrubung vorhanden Das Alter der Patienten betrug bei der Aufnahme in der Klinik 54 bis 72 Jahre 3 Patienten wussten dass sie schon seit 10 40 Jahren einen kleinen Pigmentfleck am Auge besassen nur bei 1 Patienten (Nr 4) wurde der Tumor 3 Wochen vor der Aufnahme zufallig bemerkt Bei 2 Fallen erfolgte Exstirpation des Tumors mittels Diathermie und Rontgennachbestrahlung (8000 8500 R) in 1 Fall alleinige Rontgenbestrahlung *(6150 R) und in 1 Fall (Nr 2) primare Enukleation mit* anschliessender Rontgentiefenbestrahlung (4500 R) In 2 Fallen (Nr 1 u 2) trat trotzdem innerhalb von 2 Jahren Exitus letalis ein bei Fall Nr 2 ging vorher noch eine intensive Rontgenbestrahlung und Exenteratio orbitae vor aus 1/4 Jahr vor dem Exitus letalis kam es zu einer Melanomaussaat auf der gleichen Gesichtsseite (Abb 7) In den beiden *ubrigen Fallen trat innerhalb der* nachsten 6 bzw 8 Jahre kein Rezidiv auf allerdings erblindeten die Augen offenbar als Folge der Rontgenbestrahlung Bei Fall Nr 4 entwickelte sich eine Rontgenkatarakt und Sekundar Glaukom Das Auge wurde 4 Jahre spater wegen Beschwerden enukleiert der histologische Befund ergab kein Tumorrezidiv nur fibroses Narbengewebe im Bereich des ursprunglichen Tumorsitzes

Die hier erhobenen Befunde bestatigen erneut dass die Diagnose der Benignitat eines Pigmenttumors so lange keine Schwierigkeiten bereitet wie der Tumor nur 3 4 mm gross ist kein Wachstum zeigt und im jugendlichen Alter beobachtet wird Wesentlich schwieriger wird es bei Zunahme der Pigmentie

Tabelle 1

krbl Nr	Geschl	Alter	Zeitdauer	histol Besonderh	Behandlung	Besonderheiten	Nachbeobachtung
253/1956 klinisch Melanomverdacht	♂	5 J	4 J	Pigmentzellnaevus Melanomverdachtig	Exstirpation	3 mm grosser Pigmentknoten mit starkem Umgebungsodem und Gefasszeichnung	10 Jahre
708/1960	♂	20 J	1 J	Pigmentzellnaevus	Exstirpation	4 mm grosser Knoten am Korper mehrere Pigmentnaevi	ungekannt
605/1961	♀	7 J	3 J	Pigmentzellnaevus	Exstirpation	3 mm grosser Knoten mit vermehrter Gefasszeichnung	5 Jahre
220/1962 klinisch Melanomverdacht	♀	21 J	2 3 J	Pigmentzellnaevus Melanomverdachtig	Exstirpation mittels Diathermie	Graviditas Mens VI In letzten Wochen Zunahme der Pigmentierung 4 5 mm Grosse	7 Jahre
1306/1963 klinisch Melanomverdacht	♂	32 J	3 J	Pigmentzellnaevus mit chronischer Entzundung	8000 R OD Ro Bestrahlung Exstirpation	5 mm grosser Tumor stark durchblutet Verdacht auf Malignitat Nach 3 J beginnende Ro Cat Nach 4 J Chorioretinitis mit grossem zentralem atrophischen Aderhaut Netzhaut Herd kleine Netzhautblutungen und ciremataartige Herde und Gefassneubildungen in der Umgebung SFT 1 168 AST 400	4 Jahre

1314/1963	♀	14 J	1 J	Pigmentzellnaevus mit chron. Entzündung am Rande	Rö Bestrahlung 5400 R OD Exstirpation	4 mm grosser Knoten auf der Karunkel	4 Jahre
1317/1963	♂	6 J	½ J	Pigmentzellnaevus mit chronischer Entzündung	Exstirpation	2,5 mm grosser Knoten mit vermehrter Gefässzeichnung am Rande	3 Jahre
1104/1965	♂	21 J	½ J	Pigmentzellnaevus	Exstirpation	3 mm grosser Knoten	3 Jahre

Tabelle 2

Krbl Nr	Geschl	Alter	Zeitdauer	histol Besonderh
644/1958	♀	54 J	Seit 10 J kleiner roter Fleck im letzten ½ J vergrossert	Malignes Melanom
75/1959	♂	72 J	Seit 40 J nach Kriegsverletzung kleinen pigmentierten Fleck bemerkt Seit ½ J Vergrosserung	Naevuszellnester und typisches malignes Melanom
69/1960	♀	67 J	Seit 20 J stecknadelkopfgrosser Tumor seit 6 J Vergrosserung und Pigmentierung	Malignes Melanom
351/1963	♀	68 J	Seit 3 Wochen zufallig bemerkt	kein Befund

rung z B wahrend einer Graviditat (Fall Nr 4 Tab 1) und bei auffallender Gefasszeichnung und Grossenzunahme in derartigen Fallen kann unter Umstanden auch histologisch keine klare Abgrenzung gegenuber einer Malignitat erfolgen (Fall Nr 1 4 und 5 Tab 1) Andererseits ist bei Pigmenttumoren der Bindehaut im hoheren Lebensalter immer mit einer Malignitat zu rechnen wie die wenigen von uns beobachteten Falle sehr eindrucksvoll zeigen Trotz therapeutischer Massnahmen kamen 2 der 4 Patienten innerhalb von 2 Jahren ad exitum Fall Nr 2 mit einer sichtbaren metastatischen Aussaat auf der gleichen

Behandlung	Besonderheiten	Nachbeobachtung
Ro Bestrahlung 8000 R OD Exstirpation	kirschgrosser Tumor im nasalen Lidwinkel	Nach ? Jahren †
Enukleation Ro Bestrahlung 4500 R OD	Bohnengrosse rötliche Geschwulst, die den halben Limbus umgreift, kein Übergreifen auf die Conjunktiva tarsi	Nach 1 Jahr Rezidiv in der Augenhöhle Ro Vorbestrahlung 500 R, Exenteratio orbitae Nachbestrahlung der Höhle (Tiefentherapie 3000 R) und der Lymphdrüsen 3500 R OD Nach 3/4 J Aussaat von Melanomknoten linke Gesichtsseite. Ro Bestrahlung 3500 R OD †
Exstirpation Ro Bestrahlung 8500 R OD	Erbsengrosse bräunlicher Tumor mit vielen Gefässen u randnaher Hornhauttrübung Beginnende Cat. senilis An den Armen viele Warzen	8 Jahre Auge ist erblindet
Ro Bestrahlung 6150 R. OD	5 mm grosser hellbrauner an 1 Stelle dunkelbraun pigmentierter Tumor am Limbus mit vielen Gefässen und randnaher Hornhauttrübung	Nach 2 Jahren fortgeschrittene Cataract und Sekundär Glaukom Amaurose 6 Jahre Beobachtung Nach 4 Jahren Enukleation. *Histol* kein Antalt mehr von Tumorzellen

Gesichtsseite – Bemerkenswert ist dass bei 3 der beschriebenen malignen Melanome schon seit 10 40 Jahren ein Pigmentfleck in der Konjunktiva beobachtet wurde und in Fall 2 auch histologisch der Charakter eines Pigmentzellnaevus nachzuweisen war Diese Beobachtungen weisen erneut daraufhin wie *entscheidend wichtig es ist dass auch kleine Pigmenttumoren u einem Zeitpunkt entfernt werden wo sie noch als benigne anzusehen sind also möglichst im jugendlichen Alter* Dabei kann die einfache Exstirpation – eventuell ergänzt durch Diathermie oder gleichzeitige Kryobehandlung – genügen wie sich

Tabelle 2

Krbl Nr	Geschl	Alter	Zeitdauer	histol Besonderh
644/1958	♀	54 J	Seit 10 J kleiner roter Fleck im letzten 1/2 J vergrossert	Malignes Melanom
75/1959	♂	72 J	Seit 40 J nach Kriegsver letzung kleinen pigmen tierten Fleck bemerkt Seit 1/ J Vergrosserung	Naevuszellnester und typisches malignes Mela nom
69/1960	♀	67 J	Seit 20 J stecknadelkopf grosser Tumor seit 6 J Vergrosserung und Pig mentierung	Malignes Melanom
351/1963	♀	68 J	Seit 3 Wochen zufallig bemerkt	kein Befund

rung z B wahrend einer Gravidität (Fall Nr 4 Tab 1) und bei auffallender Gefasszeichnung und Grossenzunahme in derartigen Fallen kann unter Um standen auch histologisch keine klare Abgrenzung gegenuber einer Malignitat erfolgen (Fall Nr 1 4 und 5 Tab 1) Andererseits ist bei Pigmenttumoren der Bindehaut im hoheren Lebensalter immer mit einer Malignitat zu rechnen wie die wenigen von uns beobachteten Falle sehr eindrucksvoll zeigen Trotz thera peutischer Massnahmen kamen 2 der 4 Patienten innerhalb von 2 Jahren ad exitum Fall Nr 2 mit einer sichtbaren metastatischen Aussaat auf der gleichen

Behandlung	Besonderheiten	Nachbeobachtung
Ro Bestrahlung 8000 R OD Exstirpation	kirschgrosser Tumor im nasalen Lidwinkel	Nach 2 Jahren. †
Enukleation Ro Bestrahlung 4500 R OD	Bohnengrosse rotliche Geschwulst die den halben Limbus umgreift kein Übergreifen auf die Conjunktiva tarsi	Nach 1 Jahr Rezidiv in der Augenhohle Ro Vorbestrahlung 500 R Exenteratio orbitae Nachbestrahlung der Hohle (Tiefentherapie 3000 R) und der Lymphdrusen 3500 R OD Nach 3/4 J Aussaat von Melanomknoten linke Gesichtsseite. Ro Bestrahlung 5500 R OD †
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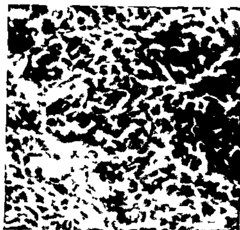


Abb 4
Histologischer Befund vom Pigmentzellnaevus mit typischen Naevuszellnestern
(Fall 7 Tab 1)



Abb 5
Melanom im ausseren Lidwinkel und am Limbus Durch Rontgenbestrahlung geheilt
(Fall 4 Tab 2)

aus der langeren Überwachung unserer Patienten mit Pigmentzellnaevi (Tab 1) ergibt Besteht die Moglichkeit der β Bestrahlung so ist sie auf Grund ihrer guten Ergebnisse vorzuziehen

Noch einige Bemerkungen zur Rontgentherapie maligner Tumoren im äusseren Augenbereich Um mit der konventionellen Rontgenbestrahlung



Abb 6
Rezidivtumor nach *Enukleation und Rontgennachbestrahlung* (Fall 2 Tab 2)



Abb 7
Metastasenaussaat linke Gesichtsseite 3/4 Jahr nach Exenteratio orbitae (Fall 2 Tab 2)

(Chaoul sche Nahbestrahlung) bei epibulbaren Melanomen einen uberzeugenden Erfolg zu erzielen sind sehr hohe Dosen von moglichst 6 8000 R Oberflachen *dosis (OD) notwendig Da uns keine andere Strahlenbehandlung zur Verfugung* stand wurde sie bei den 4 malignen und 2 fraglich benignen Fallen eingesetzt In 2 Fallen konnte der Exitus letalis nicht verhindert werden da wahrschein lich schon Metastasen bestanden die allerdings zur Zeit der Behandlung kli nisch nicht ermittelt wurden In den ubrigen Fallen konnte ein ausreichender therapeutischer Erfolg quoad vitam bei 6 – bis 8 jahriger Nachbeobachtungs zeit festgestellt werden – allerdings nicht quoad visum

Bei 5 der 6 bestrahlten Falle kam es in den folgenden 2 4 Jahren zur prak



Abb 8
Histologischer Befund des Primärtumors Gomori Färbung (Fall 2 Tab 2)

tischen Erblindung der Augen In 1 Fall musste wegen Schmerzen und Sekundärglaukoms das bestrahlte Auge enukleiert werden – Tumorzellen waren histologisch nicht mehr nachzuweisen

Bei einem Fall (Nr 5 der Tab I) entwickelten sich Veränderungen wie sie heute nur noch sehr selten gesehen werden und bei Unkenntnis der Vorgeschichte zu differentialdiagnostischen Schwierigkeiten führen können So wurde 3 Jahre nach der Röntgenbestrahlung (8000 R OD in 36 Sitzungen) eine beginnende Röntgenkatarakt mit hinterer Schalentrübung und oberflächlicher Hornhauttrübung mit Gefässeinsprossung sowie Irisatrophie temporal in Nähe des bestrahlten Bezirkes d h des früheren Sitzes des Tumors beobachtet Am Fundus bestand das Bild einer Periphlebitis retinae mit Einscheidung einiger kleiner Venenäste und winzigen Blutungen in der Umgebung im temporalen und oberen Bereich 1 Jahr später hatte sich am Fundus im Bereich des hinteren Pols ein mehrere papillendurchmessergrosser atrophischer Aderhaut Netzhautherd entwickelt der von breiten circinataartigen Degenerationen umgeben war In der gesamten Funduspheripherie befanden sich einzelne kleine retinale Blutungen mit mehreren feinen Gefässneubildungen und gröberen weissen Einscheidungen der Vena temporalis inferior und einzelner kleiner Venenäste (Abb 9) Die Hornhaut Iris und Linsenveränderungen hatten kaum zugenommen Der Visus betrug noch 1/20

Ähnliche Strahlenschäden am Fundus wurden von *Birch-Hirschfeld* 1904 7 *Hoffmann* 1930 *Schmidt* 1937 *Fry* 1952 *Schreck* 1953 *Winter u Mitarb* 1958 *Fleming* 1962 *Chee* 1968 u a mitgeteilt Sie traten nach Röntgenbestrahlungen bulbärer, orbitaler und palpebraler Tumoren aber auch nach Hypophysenbestrahlungen auf Meistens werden die Schäden am Fundus allerdings nicht diagnostiziert da durch eine Strahlenkatarakt der Einblick in den hinteren Augenabschnitt gestört ist und das Auge an einem Sekundärglaukom zugrunde geht



Abb 9
Rontgenspatschaden am Augenhintergrund mit atrophischem Aderhauterd am hinteren Pol und circinataartigen Degenerationen in der Umgebung Gewebseinscheidung der Vena temp inferior (Fall 5 Tab 1)

Es ist deshalb sehr zu erwagen ob man heute noch eine Rontgenbestrahlung mit Oberflachendosen von 8000 R und mehr am Auge selbst anwenden soll Eine sofortige Enukleation bzw Exenteratio orbitae kann dem Patienten viele Beschwerden ersparen und die Moglichkeiten eines gunstigen Ausganges *quoad vitam* steigern Die weitere Entwicklung der Strahlentherapie lasst erwarten dass derartige Schaden am Auge auch bei der Hypophysenbestrahlung immer seltener werden Fur epibulbare Tumoren hat die β Bestrahlung einen wesentlichen Fortschritt gebracht da *sie eine starke Oberflachenwirkung mit schnellem* Dosisabfall zur Tiefe besitzt und die hinteren Augenabschnitte kaum gefahrdet *Mallet* (1965) empfiehlt die Behandlung mit Radiumkornern in Form von seeds (4000 R innerhalb von 48 72 Stunden) wobei allerdings eine Strahlenkatarakt in Kauf *genommen wird die 3 bis 5 Jahre spater zu operieren ist*

Zusammenfassung

Der Naevus pigmentosus ist die haufigste Pigmentgeschwulst im Bereich der Bindehaut und wird vor allem im jugendlichen Alter beobachtet Da er des ofteren maligne *entartet ist seine fruhzeitige* Entfernung dringend erforderlich Das maligne Melanom tritt meistens im Alter auf Trotz Totalexstirpation bzw Enukleation und Exenteratio orbitae und Rontgenbestrahlung ist der letale Ausgang *nicht* immer *zu* verhindern Die Rontgenbestrahlung epibulbarer Tumoren ist wegen ihrer Gefahren fur den Bulbus kein adaquates *Verfahren*



Abb 8
Histologischer Befund des Primartumors Gomori Farbung (Fall 2 Tab 2)

tischen Erblindung der Augen in 1 Fall musste wegen Schmerzen und Sekundarglaukoms das bestrahlte Auge enukleiert werden – Tumorzellen waren histologisch nicht mehr nachzuweisen

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From the Department of Ophthalmology Kommunehospitalet Copenhagen Denmark (Heads P Brændstrup and M S Norn)

DENDRITIC (HERPETIC) KERATITIS

IV Follow Up Examination of Corneal Sensitivity

BY

M S NORN

The corneal sensitivity may be impaired in various diseases of the cornea e g corneal dystrophy (Fuchs endothelial dystrophy Groenow s macular dystrophy rarely the granular) following zoster ophthalmicus in trachoma at the site of blood vessel invasion after cataract extraction at the site of the transected nerves etc

Corneal ulcer is associated with hyperaesthesia, whereas in the presence of attending corneal oedema hypaesthesia is found

When contact lenses are fitted a considerable reduction of the corneal sensitivity indicates that the lens ought to be modified

As is well known the cornea is often hypaesthetic after herpetic keratitis According to *Thygeson et al* the impaired sensitivity is an important diagnostic sign the sensitivity being always reduced in these cases often even greatly so

Severin on the other hand has shown the sensitivity to be normal in cases of purely epithelial stellate keratitis Purely epithelial dendritic keratitis is certainly associated with impaired sensitvity during an eruption but the sensitivity returns to normal in the course of about 8 months The sensivity becomes more

Aided by a grant from *Cykelhandler P Th Rasmussen og hustru Alma Rasmussen s mindelegat*

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mehr Es wird in diesem Zusammenhang über schwere Schaden am Augenhintergrund berichtet

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impaired in relation to deeper herpetic keratitis and remains at this low level (27 eyes observed for up to 12 months)

According to *Gundersen* the sensitivity is not impaired at the start of the first attack but the impairment develops in the course of this

The cause of the impaired sensitivity has been discussed

Reiser on histological examination of rabbit corneae found no primary damage of the corneal nerves at the acute stage Here and there he noticed it is true a coat of leucocytes round the nerves but similarly may be seen in other forms of keratitis (vaccinia serpiginous ulcer) The phenomenon is probably due to the leucocytes penetrating the easiest into the cornea along the nerves

The impaired sensitivity in dendritic keratitis is in Reiser s opinion due to oedema especially in the limbal region whereas there is found no proper neuritis in the cornea

Gruter (quoted by Severin and Reiser) however claims to have observed inflammation of corneal nerves at an early stage of the disease by means of a special staining technique methylene blue Further *Nakajima* (quoted by Reiser) found irregular thickening of brain stems in the cornea on examination in the slit lamp

If Reiser s theory is correct the corneal hypaesthesia should be rather diffusely extended over the whole cornea *Holwich* stated in fact that the sensitivity was reduced throughout the cornea the impairment being not limited to the dendritic process *Boberg-Ans* and *Severin* on the other hand noticed a more or less localized impairment of sensitivity

According to Reiser s theory normalisation of the sensitivity should be expected gradually as the disease improves and the oedema subsides

In agreement with this *Sood* found improvement of the sensitivity in the few cases of dendritic keratitis subjected to follow up examination with a cotton wisp

Severin however using Cochet & Bonnet s sensibilometer saw no improvement in the patients whose disease was located under Bowman s membrane Severin is accordingly of the opinion that the disease is concentrated primarily in the corneal nerves and depends on the neurovirulence of the herpes virus

The corneal sensitivity seems to be of prognostic value The more impaired it is the greater is the chance of recurrence (*Paton* *Simkova* (quoted by Severin) *Severin*)

Various unclarified questions are thus attached to the corneal sensitivity after dendritic keratitis How often is the sensitivity impaired after dendritic keratitis? Does the sensivity improve after many years or is the impairment stationary? It the impaired sensitivity mainly diffuse or localized?

An attempt has been made to answer these questions by a follow up of 10? patients The composition of the series as well as the observation period recur

rence rate incidence of corneal opacity blood vessel invasion Hudson Stahli s line visual impairment vital staining of the cornea and Fischer Schweitzer s fluorescein pattern have been dealt with in three previous papers (*Norn* 1969)

Method

Measurement of the corneal sensitivity with a nylon thread of variable length was introduced by *Boberg Ans*

Cochet & Bonnet s sensibilometer was used for the present study A nylon thread is passed so as to touch the cornea at right angles to this The thread may be varied in length so that the presure applied against the cornea may range from 11 mg/0 0113 mm² to 200 mg/0 0113 mm²

The measurements are performed with the patient sitting on a chair and fixing a point above eye height There is a fairly strong light on the cornea allowing one to see exactly which point of this is touched and to control at which moment the thread touches the cornea and therefore becomes slightly curved

A curving of less than 5 % is aimed at (*Cochet & Bonnet*)

One starts with maximum thread length corresponding to the lowest pressure (11 mg) and thereafter reduces the thread length at the following touches until the length at which the patient is just able to feel the touching The thread length is read and converted into mg/0 0113 mm² by the aid of the table supplied by the firm

The apparatus used can only measure values within the range of 11 to 200 mg/0 0113 mm This means that an extremely high corneal sensitivity is recorded as 11 mg while asensitivity and a very pronounced hyposensitivity are recorded as 200 mg at most i e less than the true value

The applications are performed at a slow rate to avoid summational effect In the present series measurement was made first at the centre of the cornea and then at different points in the periphery attention having been concentrated on perimetering a possible localized hyposensitive region

If the assessments were unreliable the measurements were repeated some times

The contralateral eye was examined in the same manner

Result

The mean result of the sensitivity measurements at the centre of the cornea is shown in Table I The sensitivity was greatly impaired in the eye which had been affected with dendritic keratitis

Table I

Mean corneal sensitivity centrally on the cornea in 107 patients with previous dendritic keratitis measured with Cochet & Bonnet s aesthesiometer expressed in mg 0 0113 mm² (Thread diameter 0 12 mm)

	No of corneae	sensitivity	
		kerat aff eye	contralat. eye
unilateral	96	83	19
bilateral	22	49	-
Total	118	77	19

The weight on the cornea required for the touching to be recognized was on an average four times that on the cornea of the contralateral eye

By way of comparison it may be mentioned that *Cochet & Bonnet* take a difference in sensitivity exceeding 20 30 % between the right and the left eye of a patient to be pathological

The investigation comprised 118 corneae from 96 patients 11 patients having had bilateral dendritic keratitis

In 81 per cent of the 96 unilateral cases a marked difference (over 30 %) was found between the two eyes with impaired sensitivity of the keratitis affected eye Unlike in the control eye a minimum weight of 5 mg or more was required in this eye before the touching was recognized (5 10 mg in 17 per cent 11 24 mg in 1 per cent 25 51 mg in 11 per cent 52 64 mg in 15 per cent 65 134 mg in 26 per cent and more than 134 mg in 11 per cent)

In 4 per cent the difference between the two eyes was doubtful being less than 5 mg In 13 per cent the two corneae were equally sensitive and in 2 per cent hypaesthesia was found in the contralateral eye

In one of the two cases with sensitivity findings contrasting with those to be expected the measurement of the keratitis affected eye gave 75 mg and that of the contralateral eye 145 The latter eye presented a thick elevated bandular degeneration after injury which explains the impaired sensitivity

In the other case measurement gave 13 mg in the keratitis affected eye against 21 mg in the contralateral eye In this case no explanation could be given of the impaired sensitivity in the contralateral eye

The central corneal sensitivity of the contralateral eye averaged 19 mg By way of comparison it may be mentioned that Cochet & Bonnet using the same apparatus found it to average 11 6 mg in 112 normal eyes

The sensitivity was maximal i e measured at 11 mg in most cases of the present series In 28 per cent it was impaired in 5 per cent even greatly so In these latter cases a possible explanation could be given of the pronounced im pairment sequela of cataract extraction iridencleisis *corneal dystrophy* opa city of unknown cause and finally bandular corneal degeneration following injury seen in one case

Site

Localized hypaesthesia was found in 48 per cent of 118 corneae

The hypaesthesia was limited to the central region in 12 per cent The sen sitivity was often greatly impaired e g corresponding to 145 mg centrally against 21 mg at the inner periphery and 13 mg quite peripherally

In 14 per cent the impaired sensitivity was limited to a peripheral fairly small often sector formed region In the remaining 22 per cent about half of the cornea was particularly hypaesthetic

In the other 52 per cent the corneal sensitivity was uniformly impaired or normal or it was mildly and uniformly impaired along the whole periphery compared with the central region as is seen in normals (*Cochet & Bonnet*)

If in the above statement (table I) the lowest sensitivity recorded indepen dently of its site on the cornea had been employed instead of the value for the central part of the cornea a greater difference from the mean value for the control eye would have been found It may however in some cases be dif ficult to decide whether a reduced sensitivity peripherally represents the norm ally occurring lower sensitivity in this region or whether it is due to a patho logical process On this account only the central value is counted

Age and Sex

The report given below comprises only the 96 unilateral cases to render pos sible a direct comparison of the keratitis affected eye with the contralateral which acts as control

Table II illustrates the dependence of the sensitivity on age The sensitivity was seen to decrease markedly with increasing age both in the keratitis af fected eye and in the control eye

A similar fall has been described in normal series after the age of 40 50 (*Boberg Ans*) In the present series such a fall was perhaps seen from the age of 30 It was pronounced in the keratitis affected group where the age deter mined reduction of sensitivity was added to the pathologically impaired corneal sensitivity

No significant sex difference was demonstrable

Table II

Possible dependence of corneal sensitivity on age and sex in dendritic keratitis affected and in contralateral eye Sensitivity given in mg 0 0113 mm²

age	number	sensitivity	
		kerat aff eye	contralat eye
0– 9	16	61	12
10–19	10	59	12
20–29	12	75	11
30–39	12	88	17
40–49	20	79	22
50–59	14	100	21
≧ 60	12	124	35
females	40	77	23
males	56	88	15
Total	96	83	19

Observation Period

The corneal sensitivity was measured in connection with a follow up of patients who had previously had dendritic keratitis

The first attack had occurred not less than 5 years – on an average 13 years – before the follow up

The patients who had had only one attack have been collected in table III

The impaired sensitivity in the keratitis affected eye seemed to be independent of the length of the observation period Especially no improvement of the sensitivity was seen in cases with a particularly long observation period

Recurrence

Patients who had had many relapses showed a strikingly low corneal sensitivity whereas patients with only few relapses had a better sensitivity (fig 1)

The contralateral eye on the other hand showed no correlation between sensitivity and recurrence rate

Two explanations may be offered of the observed correlation between impairment of sensitivity and recurrence rate in the keratitis affected eye Either patients with a greatly impaired sensitivity at the first attack are liable to repeated relapses (cf *Severin*) or the sensitivity becomes increasingly impaired after each new attack

Table III

Corneal sensitivity compared with observation period in years 43 cases of dendritic keratitis without recurrence.

Obs period	number	corneal sensitivity (mg/0 0113 mm²)	
		kerat. aff eye	contralat eye
5– 6 yrs	14	64	14
7– 8 yrs	9	39	11
9–10 yrs	10	61	13
11–12 yrs	7	65	30
13–18 yrs	[illegible]	106	11
> 18 yrs	1	200	11

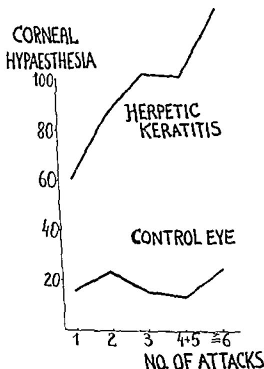


Fig 1

Correlation between number of attacks of dendritic keratitis and impairment of corneal sensitivity

Abscissa number of attacks

Ordinate mean corneal sensitivity expressed in mg 0 0113 mm²

Upper curve keratitis affected eye lower curve contralateral eye

Corneal Opacity

The sensitivity was most impaired in the cases showing corneal opacity Note however that the sensitivity also was impaired in the group presenting no opacity (table IV)

The impairment seemed to be the greatest in the cases where the opacity extended the deepest into the parenchyma (table IV) On the other hand no definite correlation was demonstrable between the opaque area and the impairment of sensitivity

The impairment was most pronounced in cases with blood vessel invasion of the cornea (on an average 108 mg in 50 patients with vascularisation against 56 mg in 46 without)

No correlation was noticed between presence of Hudson Stahli s pigment line in the cornea and impaired sensitivity (82 mg in 50 patients with the line and 84 mg in 46 patients without) This is surprising because Stahli s line is a very frequent phenomenon after dendritic keratitis (*Norn* 1969 B)

The cases classified in the case records as metaherpetic showed less corneal sensitivity than the non metaherpetic (99 mg against 69 mg)

Precorneal Film and Epithelium

The impaired sensitivity was most pronounced in the cases where the corneal surface was of poor quality manifesting itself by vital staining of the epithelium with fluorescein or rose bengal (107 mg in the 35 stainable cases against 69 mg in the 61 non stainable)

The sensitivity was most impaired in the eyes having the lowest wetting time

Table IV

Possible dependence of corneal sensitivity on depth of corneal opacity 96 patients who had had unilateral dendritic keratitis

depth of opacity	number	sensitivity	
		kerat aff eye	contralat eye
no opacity	15	33	12
superfic	31	73	14
< 1/4	23	83	25
< 1/2	5	134	15
< 3/4	5	141	27
> 3/4	17	113	24

of the precorneal film (110 mg in the cases with permanently dry holes i e wetting time = zero 99 mg at wetting times from 1 to 9 seconds and only 74 mg at wetting times exceeding 29 seconds)

The patients with a pathological Fischer Schweitzer s fluorescein pattern had the most impaired corneal sensitivity (90 mg in 76 patients with a pathological pattern against 58 mg in 20 with a normal pattern) cf *Vorn* 1969 C

Vital staining discloses defects and degeneration of the corneal epithelium the wetting time depends presumably on the epithelial layer of fat and Fischer Schweitzer s fluorescein pattern reflects sequelae of a pathological process close to Bowman s membrane We do not know for certain whether the pheno menon is connected with structures deep to or superficial to the membrane.

Signs of present or previous pathological conditions in these superficial cor neal layers may thus be correlated to the degree of sensitivity impairment though a causal relationship is unlikely where the most superficial phenomena are concerned

Impaired corneal sensitivity was more pronounced among the patients with signs of previous iritis (125 *mg in 28 patients) than among the patients with* out such (66 mg in 68 patients)

No correlation or perhaps rather a slight negative correlation was found between sensitivity impairment and previous or present affection with herpes of *the lips* (79 *mg in* 46 patients with herpes against 8[illegible] mg in 50 patients without)

Visual Acuity

Table V gives a survey of the visual acuity at the follow up in relation to the

Table V

Corneal sensitivity compared with visual acuity of keratitis affected eye at the follow up Sensitivity given in mg 0 0113 mm²

visual acu ty	number	sensitivity	
		kerat aff eye	contralat. eye
< 6 36	9	154	27
< 6/18	10	116	27
< 6 9	27	92	20
< 6 6	16	8[illegible]	13
≥ 6 6	34	50	15
Total	96	83	19

impairment of sensitivity A positive correlation was seen between the impairment of vision and that of sensitivity The poorer the vision the more impaired was the sensitivity The control eye showed a slight tendency in the same direction however

Therapy

The impairment of sensitivity might be conceived to depend on the therapy given

The investigation showed no difference between the patients treated with 5 iodo 2 deoxyuridine (IDU) and those treated by iodine cauterisation (on an average 90 mg in the IDU treated and 87 mg in the iodine treated Control eye 21 and 18 mg respectively)

Impaired corneal sensivity was perhaps more pronounced amongs the patients treated with steroids (average 103 mg control eye 23 mg)

Discussion

The method employed for measuring corneal sensitivity is probably the most accurate one existing (Boberg Ans Cochet & Bonnet) The objections may be raised to this method that it is subjective that repeated examinations may give somewhat unequal results and that the range of measurements with the apparatus used is limited to 11 200 mg/0 0113 mm Hypersensitivity therefore cannot be recorded and – what is a greater disadvantage in the present investigation – more pronounced hypaesthesia than that corresponding to 200 mg and proper anaesthesia are both recorded as hypaesthesia of 200 mg This latter fact probably means that the difference between the keratitis affected eye and the control eye is greater than the tables indicate

Is the impaired sensitivity in dendritic keratitis due to neuritis caused by the herpes virus or to a more diffuse cellular infiltration with oedema as supposed by Reiser?

The impaired sensitivity was limited to a circumscribed area in 48 per cent of the present series This area was sector formed in some cases while in others about half of the cornea was hypaesthetic The localized character might be conceived to be caused by oedema which is particularly pronounced peripherally

In 12 per cent out of 118 corneae the hypaesthesia was localized centrally

This does not harmonize with the hypothesis of *oedema which according to* Reiser is most pronounced in the limbal region

According to Reiser s theory the corneal nerves *may in some instances* be injured secondarily but a permanent impairment of sensitivity must be exceptional

The present sensitivity investigation is based on a follow up We do not know the degree of sensitivity during the first attack nor at subsequent attacks or between these

The mean impairment of sensitivity seemed however to be independent of the observation period In other words the sensitivity seemed not to improve in the course of years

This fact militates against Reiser s theory The frequent and pronounced impairment of sensitivity noticed in the present series indicates a considerable action on the corneal nerves which is rather to be interpreted as a sequela of neuritis due to the herpes virus

The impaired corneal sensitivity has in this series been compared with various other parameters The impairment was found to be most pronounced in cases with concurrent corneal opacity especially deep opacity with blood vessel invasion with defects of the corneal epithelium and the precorneal film and with alterations round Bowman s membrane previous iritis grave visual impairment and increased liability to recurrence

It is difficult to see which of these factors are primary which secondary and which perhaps independent

The impaired corneal sensitivity is possibly to be regarded as a primary factor The first attack by a particularly neurotropic virus may give rise to dendritic keratitis with very pronounced hypaesthesia (cf Severin) After the first attack the hypaesthetic cornea is liable to relapses This explains why the final result after several relapses is a cornea with a deep opacity and blood vessel invasion a deficiently covering precorneal film a vulnerable epithelium with degenerate epithelial cells defect of Fischer Schweitzer s fluorescein pattern and a poor vision

How often are sequelae of dendritic keratitis detectable? (table VI)

Corneal opacity was present in 81 of the 96 patients with one eye affected In five of the remaining 15 cases a pathological Fischer Schweitzer s pattern was seen

Of the last ten patients seven had a pathological corneal sensitivity (21 75 mg in the keratitis affected against 11 mg in the control eye)

Only three patients had no detectable sequelae None of these experienced recurrence One recovered in less than 48 hours

The seven cases in which hyposensitivity was measured in one eye with no

impairment of sensitivity A positive correlation was seen between the impairment of vision and that of sensitivity The poorer the vision the more impaired was the sensitivity The control eye showed a slight tendency in the same direction however

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peripherally being sector formed while in 22 per cent it comprised half of the cornea and in the remainder it was diffuse

Declining corneal sensitivity was found to be positively correlated to rising number of relapses presence of opacity blood vessel invasion of the cornea stainability of the cornea reduced wetting time defects or absence of Fischer Schweitzer fluorescein pattern previous iritis and increasing impairment of vision It is possibly correlated to increasing depth of corneal opacity

The corneal sensitivity seems not to be correlated to the length of the observation period nor to presence of Hudson Stahli s line, and hardly to herpes of the lip

Sequelae of dendritic keratitis (opacity pathological Fischer Schweitzer s fluorescein pattern impaired sensitivity) were not visible in three of the 96 corneae

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Table VI
Sequelae of dendritic keratitis in per cent

corneal opacity	85
blood vessel invasion	50
Hudson Stahli s line	52
pathol Fischer Schweitzer s pattern	79
hyposensitivity	81
opacity and/or pathological Fischer Schweitzer	90
opacity and/or pathological Fischer Schweitzer and/or hyposensitivity	97
no sequelae	3

other pathological findings are interesting because such cases may cause differential diagnostic difficulties within neuro ophthalmology if a history of previous keratitis is not available

It is remarkable that no more than 3 per cent completely avoided recognizable sequelae of dendritic keratitis

The series under review is in some measure selected in as far as it exclusively comprised patients referred to an ophthalmic out patient clinic However the thorough clinical examination must be supposed very frequently to disclose sequelae of dendritic keratitis even in a non selected series

The results of the present study bore out the theory that measurement of the corneal sensitivity *gives information of prognostic value in dendritic keratitis*

Summary

A series of 96 patients who had had their first attack of unilateral dendritic keratitis not less than 5 years previously – on an average 13 years previously – had their corneal sensitivity measured with a nylon thread according to Boberg-Ans using Cochet & Bonnet s apparatus

In 81 per cent the sensitivity was markedly impaired compared with that of the contralateral eye The average pressure required for the touching to be recognized was four times higher on the keratitis affected eye than on the contralateral

In 12 per cent the hypaesthetic region was localized centrally in 14 per cent

subcapsular layer of both lenses »A striking silvery grey delicate and com plete rosette formation of petals tracing the fine feathery architecture of ra diating lens fibers was observed Visual acuity was *not affected* Three weeks after withdrawal of Floropryl the changes had completely disappeared

Jones & Watson (1967) reported bilateral angle closure glaucoma in a 7 year old boy treated with 0 125 % Phospholine Iodide for an accommodative convergent squint. The tension was quickly normalized by atropine ointment but isolated gonio synechiae persisted

The present paper will describe some side effects observed in a group of young persons with various types of accommodative convergent deviations who were subjected to Floropryl or Phospholine Iodide therapy

Material and Methods

The material consisted of seven boys aged 4 12 years and eleven girls or young women aged 6 23 years A young woman aged 19 was treated with 0 1 % Floropryl twice daily for three months whereas the other 17 patients were treated with Phospholine Iodide as a rule twice daily and in the concentra tion of 0 06 % for periods varying from two to eight months

Before treatment was begun the lenses were examined under mydriasis with a slit lamp During treatment the patients were examined as a rule once a month At first the anterior segment of the eye was examined whereafter the pupil was dilated with 10 % Neo synephrine and the lenses examined

Seventeen of these 18 patients were re examined 6 10 months after discon tinuance of treatment using the procedure described above

Results

1 *Lenticular changes* Transient lens clouding was observed in the following two cases

Case 1 L.H ♀ aged 19 and treated with 0 1 % Floropryl twice daily O U Before therapy was started only a few solitary vacuoles were seen in the lenses After three months of treatment bilateral lens changes resembling those described by *Harrison* (1960) were observed with the exception that they appeared in both the anterior and the posterior subcapsular region There was a striking accentuation of the normal feathery architecture of the lens In oblique illumination and high magnification the bundles of lens fibers appeared swollen and were like strings of pearls In retroillumi nati n the pearls were seen to consist of very small vacuoles of about equal size Re markably enough v sual acu ty was not reduced. There were also iris cysts b laterally

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SIDE EFFECTS FROM USE OF LONG-ACTING CHOLINESTERASE INHIBITORS IN YOUNG PERSONS

BY

UNO AXELSSON and KARL GÖSTA NYMAN

Long acting cholinesterase inhibitors such as di isopropyl fluorophosphate (Floropryl) and echothiophate (Phospholine Iodide) are widely employed not only in the treatment of glaucoma but also in the management of accommodative convergent deviations In the latter case their use is intended to reduce by inducing ciliary spasm the need for central accommodation and thereby also the central convergence impulse

In young persons the local application of long acting cholinesterase inhibitors is known to cause side effects Special attention has been directed to the frequent appearance of iris cysts These however are considered innocuous because they do not impair visual function and disappear when the treatment is discontinued Neo synephrine administered simultaneously with long acting cholinesterase inhibitors has been reported to diminish cyst formation without reducing the effect on the ciliary muscle

Long acting cholinesterase inhibitors given to glaucoma patients have been shown to initiate or precipitate cataract formation (cf *Axelsson* & *Holmberg* 1966 *Axelsson* 1969) So far only *Harrison* (1960) has reported the appearance of lens opacities in young persons on administration of these drugs A 13 year old girl with accommodative esotropia who was treated with Floropryl 0 025 % bilaterally, developed after three months of treatment changes in the anterior

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* Neo synephrine® = metaoxedrine (Winthrop U S A)

of the iris may develop It is possible that this side effect might have been pre vented if Neo synephrine had been administered simultaneously with Floropryl or *Phospholine* Iodide

As previously mentioned angle closure precipitated by Phospholine Iodide has been reported by *Jones & Watson* (1967) *It is* well known that administra tion of long acting cholinesterase inhibitors to glaucomatous eyes with narrow angles may cause angle closure and formation of anterior synechiae This risk must, of course be considered also in young persons with accommodative con vergent deviations who are often hyperopic and have small eyes with shallow anterior chambers In our series no signs of angle closure and rise in tension were observed It is impossible to decide whether anterior synechiae developed as gonioscopy was not performed

Many authors have reported good results when treating accommodative con vergent deviations with long acting cholinesterase inhibitors and the side ef fects were considered negligible Our material is too small to permit a statistical evaluation of the results of treatment We can only state the clinical impression that the therapeutic effect from the orthoptic point of view was far from ex cellent. We question whether the side effects of these drugs can be considered negligible It must be borne in mind that the patients treated are young and that at present it is impossible to know how their lenses and out flow systems will behave in later life As long as these facts are not known we think that long acting cholinesterase inhibitors should be used with caution in young persons

Summary

A group of 18 young persons with various types of accommodative convergent deviations and treated with Floropryl or Phospholine Iodide, was studied with regard to side effects Transient lens clouding was observed in two cases which are described in detail Iris cysts appeared in seven patients On re examination 6 10 months after discontinuance of treatment iris cysts persisted in three pa tients and in two a patchy depigmentation of the pupillary border and the surrounding iris was observed

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At this stage the Floropryl medication was discontinued and the patient was examined two weeks later The changes described had undoubtedly regressed but numerous vacuoles still persisted On subsequent examinations a gradual regression was observed and two and a half months after withdrawal of Floropryl only a few solitary vacuoles were seen This was also the case 10 months after withdrawal On the latter occasion a small iris cyst persisted in the right eye

Case 2 J T ♂ aged 6 Before treatment started both eyes displayed remnants of the pupillary membrane and less than ten solitary lenticular vacuoles Six and a half months after institution of Phospholine Iodide 0 125 % twice daily both eyes exhibited lens changes of the type described for Case 1 but less pronounced and limited to sectors of the lenses Besides iris cysts were found bilaterally The treatment was then changed to Phospholine Iodide 0 06 % twice daily One month later the changes had regressed but clusters of vacuoles were still present As at this time an allergic dermatitis had developed which was associated with the treatment Phospholine Iodide was withdrawn After another month less than ten vacuoles were observed bilaterally This applied also on re examination ten months later but iris cysts persisted in both eyes

B Iris cysts During treatment iris cysts were observed in seven cases On re examination 6 10 months after treatment was discontinued iris cysts remained in three patients Two of these were Case 1 and 2 described above In the third patient a boy aged 8 and treated with Phospholine Iodide 0 125 % twice daily for seven months nine large iris cysts were observed bilaterally seven months after withdrawal of the drug Between the cysts there was a pronounced depigmentation of the pupillary border and the surrounding iris In a girl aged 6 and treated with Phospholine Iodide 0 06 % twice daily for four months similar depigmentation but no cysts was seen eight months after cessation of therapy

C Other side effects Two patients had periods of diarrhea which however did not necessitate discontinuance of treatment Another patient suffered from disturbed sleep which disappeared when medication was stopped

Signs of angle closure were not observed but it should be pointed out that in no case was gonioscopy performed

Discussion

The most interesting observation in the present study is the transient lens clouding that occurred in two cases In both these the changes observed seem to have been identical with those described by *Harrison* (1960) It is evident that the lenses of young persons are also affected by strong cholinesterase inhibitors but are capable of recovery

It is also evident that iris cysts do not always disappear when treatment with long acting cholinesterase inhibitors is discontinued and that persistent damage

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GLAUCOMA SCREENING

A Critical Evaluation Based on Routine Tonometry among Members of the Volunteer Donor Corps of the Island of Falster (Denmark)

BY

KNUD NØRSKOV

Within the past 15 20 years reports on employment of routine tonometry for tracing glaucoma have been published in practically all parts of the world

The investigations available so far have been reviewed by *Leydhecker* (1960) *Ourgaud & Étienne* (1961) *Posner & Fogland* (1964) and recently by *Segal & Skwierczynska* (1967) in which latter publication especially the Eastern European studies are well represented and by *Pollack* (1968)

The investigations reported differ appreciably with regard to composition of population groups the screening limits chosen the diagnostic examinations employed and criteria for early establishment of the diagnosis Nevertheless the various investigators arrived at fairly equal results namely that the tracings revealed not previously recognized glaucoma in from 1 5 to 2 per cent of the subjects examined above the age of 40 These investigators worked with a glaucoma concept based on the chosen criteria of glaucoma but did not as recently proposed by *Hollows & Graham* (1966) distinguish between ocular hypertension and glaucoma with loss of function

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The obligingness of both management and members of the donor corps and the enthusiasm with which the staff of the blood bank took on the extra work of screening also contributed essentially towards carrying through the project

Originally we intended to trace glaucoma by means of applanation tonometry and ophthalmoscopy As however the great majority of the donors expressed a desire to have the testing amplified so much as to constitute a regular eye examination we decided to aim at complying with this desire to the greatest possible extent trying to solve the topical eye problems of the donors

The population group chosen comprised 2354 donors listed on May 1 1962 as active members of the volunteer donor corps of Falster The collection period was concluded on January 31 1963

The recording revealed that 265 of the donors (11 per cent) did not live on Falster but on Lolland a neighbouring island As in decency we had to offer examination to all the donors irrespective of residence we decided to keep and examine the donor corps as an entity even though this involved that we did not as originally aimed at get a section of the Falster population alone

A review of the card index of the only ophthalmic medical practitioner showed that primary glaucoma had been recognized previously in two donors (a woman aged 50 and a man aged 51) while secondary glaucoma was observed in one donor In agreement with this the prevalence of previously recognized primary glaucoma (simple) was 0 09 % while that for donors aged over 40 was 0 16 % These cases of previously recognized glaucoma were ruled out from the present investigation

The number of donors who had applanation tonometry carried through was reduced for different reasons Thus 109 donors had resigned membership within the period of investigation while we did not succeed in offering examination to 21 donors

Of the 2221 donors (94 per cent) invited to applanation tonometry 69 (3 per cent) refused

Finally an acceptable applanation tonometry could not be carried through in 191 cases The majority of these belonged to the youngest age groups Males and females were fairly equally represented Ophthalmoscopy showed normal conditions in all the donors of this group

Table 1 illustrates the age and sex distribution of the 2031 donors (86 3 per cent of the original number of donor corps members) subjected to applanation tonometry It is seen that only 1146 donors (56 per cent) were over 40 years of age and 32 over 65 The mean age was 41 years for both males and females

The withdrawals of blood took place between 8 a.m and 9 p m and 52 per cent of the donors were examined after 6 o clock p m The tonometry was carried through before the blood withdrawal except in the cases of 64 donors (3 per cent) where examination after the withdrawal had to be accepted for the sake of unrestrained performance of the withdrawal

Since this publication a number of the writers concerned have felt called upon to recommend glaucoma screening to the greatest possible extent by means of tonometry, also among persons who normally have no contact with an ophthalmologist

Others hold a more critical attitude towards the problem of glaucoma screening as seen for instance in various reviews from recent years (*Hunt* 1966 *Leopold* 1967, *North* 1967, *Pollack* 1968)

This criticism has in the first place concentrated on fundamental objections to the usefulness of tonometry for tracing glaucoma at an early stage In addition, it has been concerned with the practical and financial problems arising in relation to accomplishment of routine tonometry

In an endeavour to obtain a balanced evaluation of the advantages and disadvantages of glaucoma screening among individuals with apparently normal eyes members of the volunteer donor corps of the Island of Falster have been subjected to routine tonometry, using an applanation tonometer

The series was collected in relation to a glaucoma tracing investigation carried out on Falster during the period 1960 1963

Present Material

In choosing a population group on Falster (46 662 inhabitants) which might constitute the basis of an evaluation of routine tonometry carried through on persons with apparently normal eyes it proved to be difficult to find a sufficiently large group fit to be examined as planned by a single examiner within a reasonable time Another difficulty was that of confining the examinations of such a group to a single place which was necessary owing to the use of an applanation tonometer

On Falster the prophylactic mass radiography for tuberculosis often employed for simultaneous screenings thus had an organizing form which did not allow of this combination

Further the Island of Falster has no industrial firms large enough to permit the desired limitation of routine tonometry to a single firm

This was the reason why the blood donor corps of Falster was chosen for an investigation based on routine tonometry A possibility was thereby afforded of contacting a relatively large and well organized section of the population of Falster and at the same time of carrying through the screening in one place namely the Central Hospital of Nykobing Falster where all donor blood withdrawals and donor health examinations take place

Table 2
Age and sex distribution of donors with applanation tonometric values above the screening level

Age	males	females	total	%
15–24	2	2	4	2 1
5–34	5	3	8	1 9
35–44	8	6	14	2 2
45–54	7	5	12	2 2
55–64	5	9	14	6 1
≧ 65	1	2	3	(9 4)
Total	28	27	55	2 7
	2 ? %	3 7 %		

32 donors (1 6 per cent) had values recorded of 22 mm Hg or higher and only six (0 30 per cent) values of 25 mm Hg or higher For donors aged over 40 (1146 donors) the number of donors with pressure values ≧ 20 *mm* Hg ≧ 22 mm Hg and ≧ 25 *mm* Hg *was respectively 3 4* per cent (39 *donors*) 2 0 per cent (?3 *donors*) and 0 44 per cent (5 donors)

Further Examinations

The control examinations of 55 donors comprised not only *renewed* applana tion tonometry ophthalmoscopy and determination of the central visual acuity but also visual field measurement *gonioscopy and* water provocative test. On 6 donors diurnal tension curves were obtained and 2 donors had Priscol provo cative tests carried out

The results of the further examinations of the 55 donors selected on the screening were as follows

1 Control of intra ocular pressure Six donors (nine eyes) had pressure va lues of 25 mm Hg or higher recorded

? Ophthalmoscopy 54 donors had normal optic discs One donor was seen to have a cupped disc suspicious of glaucoma in one eye

3 Visual field *measurements* These were carried out by campimetry Using object size 6/ 000 no visual field defects were detected whereas with size

Table 1
Age and sex distribution of 2031 donors subjected to applanation tonometry

Age	males	females	total
15–24	111	83	194
25–34	264	150	414
35–44	424	201	625
45–54	348	190	538
55–64	140	88	228
≥ 65	18	14	32
Total	1305	726	2031

Screening Level

It was decided that applanation tonometry showing an intra ocular pressure of 20 mm Hg or higher in one or both eyes and a difference of 4 mm Hg or higher between the right and the left eye motivated further examination with a view to presence of glaucoma

Applanation tonometric Values Below the Screening Level

In 1976 donors applanation tonometry gave values below 20 mm Hg in both eyes with a difference of less than 4 mm Hg between the right and the left eye. Thus the tonometry aroused no suspicion of glaucoma in these donors On ophthalmoscopy all the optic discs were characterized as normal

Applanation tonometric Values Above the Screening Level

55 donors (2 7 per cent) had an applanation tonometric value above the screening level measured in one or both eyes The age and sex distribution is seen in table 2 An intra ocular pressure above the screening level was more frequently measured in women than in men (3 7 and 2 2 per cent respectively) Within the age groups from 18 to 54 years the donors with pressure values above the screening level constituted approximately 2 per cent This percentage was considerably higher (6 1) for donors between the ages of 55 and 64

Table 9
Age and sex distribution of donors with applanation tonometric values above the screening level

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	2 2°/o	3 7°/o		

32 donors (1 6 per cent) had values recorded of 22 mm Hg or higher and only six (0 30 per cent) values of 25 mm Hg or higher For donors aged over 40 (1146 *donors*) the number of donors with pressure values ≧ 20 mm Hg ≧ 22 mm Hg and ≧ 25 mm Hg was respectively 3 4 per cent (39 donors) 2 0 per cent (23 donors) and 0 44 per cent (5 donors)

Further Examinations

The control examinations of 55 donors comprised not only renewed applanation tonometry ophthalmoscopy and determination of the central visual acuity but also visual field measurement *gonioscopy and water provocative test.* On 6 donors diurnal tension curves were obtained and 2 donors had Priscol provocative tests carried out

The results of the further examinations of the 55 donors selected on the screening were as follows

1 Control of intra ocular pressure Six donors (nine eyes) had pressure values of 25 mm Hg or higher recorded

2 Ophthalmoscopy 54 donors had normal optic discs One donor was seen to have a cupped *disc suspicious* of glaucoma in one eye.

3 Visual field measurements These were carried *out by campimetry Using* object size 6/2000 no visual field defects were *detected* whereas with size

2/2000 visual field defects were observed in two donors (three eyes) It was in all three eyes a question of incipient defects – baring of the blind spot. Oph thalmoscopy showed two of the eyes to have normal optic discs In the third eye the visual field defect noticed occurred in the only eye with a glaucoma suspicious optic disc

4 Gonioscopy In all the donors subjected to further examination the cham ber angle was characterized as open in principle

5 Provocative tests

a Water provocative test 54 donors (108 eyes) were subjected to this test A rise of 8 mm Hg or higher was released in 14 eyes or in 13 0 per cent of the water provocative tests A detailed account of the experience gained from the water provocative test in the present series of screening examinations has been given in a previous paper (*Nørsl ov* 1967a)

b Priscol provocative test No more than two donors were subjected to this test A rise of 11 mm Hg or higher was released in one case A detailed account of the usefulness of the priscol provocative test in the present series of screen ings has been given in a previous report (*Nørskov* 1966)

Simple Glaucoma

One or more of the following criteria were required for establishing a diagno sis of glaucoma 1 Distinct peripheral cupping of the optic disc (not met with in the present study) 2 Reproducible glaucomatous visual field defects 3 In tra ocular pressures of 25 mm Hg or higher 4 A rise of 8 mm Hg or higher in response to water provocative test 5 A rise of 11 mm Hg or higher in response to priscol provocative test

On this basis a likely diagnosis of simple glaucoma was made in the cases of 20 eyes (12 donors) as shown in table 3

The most frequent criterion was a pathological water provocative test (com bined with pressures exceeding 20 mm Hg) Ophthalmoscopic findings were not employed and visual field defects occurred in three cases only In three of the four cases in which the diagnosis was based on pressure measurements alone values of 30 mm Hg or higher were recorded

Eight donors had the diagnosis made for both eyes and four donors for one eye only The age and sex distribution is seen in table 4

The incidence of glaucoma among all the donors was 0 59 per cent with no difference worth mentioning between females and males None of the donors presented glaucoma at a fairly advanced stage Thus only two (0 10 per cent) had small visual field defects one in both eyes with no optic disc changes and the other in one eye where cupping of the optic disc was suspected

Table 3

Criteria for establishment of a diagnosis of glaucoma in 20 eyes of 12 donors

1 Criterion present	
pressure values ≧ 25 mm Hg	4
water provocative test ≧ 8 mm Hg	10
2 Criteria present	
pressure values ≧ 25 mm Hg + visual field defect	1
pressure values ≧ 25 mm Hg + water provocative test ≧ 8 mm Hg	3
priscol provocative test ≧ 11 mm Hg + visual field defect	1
3 Criteria present	
pressure values ≧ 25 mm Hg + water provocative test ≧ 8 mm Hg + visual field defect	1
	20

Table 4

Age and sex distribution of 12 donors with established diagnosis of glaucoma

Age	males	%	females	%	total	%
35–44	4	0 94	2	1 0	6	0 96
45–54	2	0.57	1	0.53	3	0.56
55–64	2	1 4	1	1 1	3	1 3
Total	8	0 61	4	0 55	12	0.59

Glaucoma was more frequent in the age group of 35 44 than in that of 45 54 Nevertheless only one donor – a woman aged 38 – had a diagnosis of glaucoma made before the age of 40 As might be expected the highest frequency of glaucoma was found in the age group of 55 64 (1 3 per cent) whereas no donor over the age of 65 had glaucoma For donors under the age of 40 the frequency of glaucoma was 0 11 per cent while for donors aged 40 or older it was 0 96 per cent.

In the present study the screening level was as stated set at 20 mm Hg If a level of 21 mm Hg had been chosen instead the number of donors for further examinations would have been reduced from 55 to 43 whereas no influence on the number of newly diagnosed glaucoma cases would have been noticed Setting the screening level at 22 mm Hg or higher further examination of 32 do-

nors (1 6 per cent) would have sufficed However in that case two donors corresponding to one sixth of the newly diagnosed glaucoma cases would have had no chance of getting their glaucoma disclosed by means of routine tonometry

Normals

This group comprised donors for whom the results of all control examinations of both eyes were within the normal range including pressure measurements below 20 mm Hg No more than eight of the 55 donors selected on the screening could thus be said to have both eyes normal This means that 14 5 per cent of the donors who on the screening had an applanation tonometric value of 20 mm Hg or higher recorded of one or both eyes could subsequently be registered as normal The result of the screening must accordingly be characterized as false positive

Borderline Cases

The borderline cases constituted the largest group among the donors subjected to further examination In this group we could not establish a diagnosis of glaucoma nor refute a suspicion of this on the basis of the examinations performed and the criteria chosen for evidencing the glaucoma diagnosis and the normality concept employed (see above) The group comprised 35 donors (15 males and 20 females) of whom 32 presented bilateral anomalies

The number of borderline cases constituted 1 7 per cent of the total number of donors subjected to routine tonometry

Discussion

The results of the routine tonometries reported above showed in agreement with previous glaucoma screenings that tonometry may reveal not previously recognized glaucoma in persons with apparently normal eyes

The frequency of glaucoma noted in the present study where 0 59 per cent of all the donors examined and 0 96 per cent of those aged 40 or older had a diagnosis of glaucoma established was lower than the usually stated 1 5 and

2 per cent for persons aged 40 or older This difference is possibly due to pre dominance of the fairly young age classes in the population group under re view and also to the fact that half of the donors had blood withdrawn after working hours having consequently been subjected to tonometry at a glauco ma prophylactically unfavourable time of the day

However a review of Scandinavian reports on routine tonometry of persons with apparently normal eyes has shown that these examinations also gave a lo wer glaucoma frequency than the often stated 1 5 to 2 per cent for persons aged 40 or older (table 5)

In the three reports on tonometry of hospitalized patients the frequency was even 0 5 to 0 6 per cent Possible explanations of the stated low frequency are discussed in a previous paper (*Nørskov* 1967b) Among these the well known fall of the intra ocular pressure during stay in hospital is pointed out

To attain to a balanced evaluation of the glaucoma prophylactic contribution yielded by subjecting persons with apparently normal eyes to routine tonome try we must however compare the results achieved in the form of newly de tected cases of glaucoma in its widest sense with the disadvantages noticed of carrying through a glaucoma screening based on tonometry

In arranging a glaucoma tracing examination using tonometry among per sons who normally have no contact with an ophthalmologist it must be ra tional from a social aspect to aim at associating the glaucoma screening with a prophylactic examination in progress (e g a campaign against tuberculosis) or at concentrating the screening on other well organized population groups (in industrial plants institutions or hospitals) This is to avoid construction of an independent organisation for prophylactic measures against a single eye disease

The reported examination on the Island of Falster showed however that it may be difficult to carry through such an association without at the same time reducing the glaucoma prophylactic value of the examination Thus the mem bers of the Falster donor corps presented a – from a glaucoma prophylactic aspect – undesirable predominance of fairly young persons (44 per cent under 40) and only one third of the examined donors were women A similar age and sex distribution has been observed in glaucoma screenings carried through at places of work (*Leydhecker* 1959 *Dersh* 1961 *Pur* 1964 *Bertelsen et al* 1965) In the cases of population examinations where routine tonometry is offered to a population aged 40 or older within a geographically well defined region a fairly small attendance among the elderly and the most exposed section of the population must likewise be accepted (*Stromberg* 1962 *Hollows & Graham* 1966)

In a coupling of this kind where as in the present study a large proportion of the donors (52 per cent) attended in the evening after working hours we must further accept a determination of the intra ocular pressure at an unfa vourable time of the day from a glaucoma prophylactic aspect

Table 5

Scandinavian routine tonometries among persons with apparently normal eyes outside the sphere of action of the ophthalmologist

	number	age	screening level (calibration table)	suspects	%	Glaucoma detected (previously unknown)					
						glaucomatous field loss	%	early glaucoma	%	total	%
Koskenoja & Orma (1955) (home for aged)	600	> 64	≧ 25 mm Hg (≦ 3 5/5 5) (1948)	83	13 8	–	–	–	–	15	2 5
Katavisto & Sammalkivi (1964) (non ophthalmological in patients)	5760	≧ 40	≧ 20 5 mm Hg (≦ 4 0/5 5) (195[illegible])	391	6 8	–	–	–	–	24	0 5
Nørskov (1967) (non ophthalmological in patients)	314	≧ 35	≧ 20 5 mm Hg (≦ 4 0/5 5) (1955) ≧ 20 mm Hg appl	12	3 8	1	0 32	1	0 32	2	0 64
Jensen (1968) (non ophthalmological in patients)	1051	> 40	≧ 22 mm Hg (≦ 3 5/[illegible] 5) (1955)	34	3 2	–	–	6	0 6	6	0 6
Stromberg (1962) (total population)	7275	≧ 40	> 20 5 mm Hg (< 4 0/5 5) (195[illegible])	325	4 5	11	0 15	–	–	–	–
Bertelsen et al (1965) (industrial workers)	1909 (1108)	> 19 > 40	≧ 20 5 mm Hg (≦ 4 0/[illegible] 5) (19[illegible])	144	7 [illegible]	3	0 16	12	0 6	1[illegible] 1[illegible]	0 8 1 4

The population is greatly interested in prophylactic examinations when such are offered in a well organized form Thus for instance the offered tonometry was refused by less than 5 per cent of the donors concerned

However the effectiveness of a glaucoma screening depends not only on the attendance at the primary screening but also on the extent to which suspects after the first screening really are prepared to submit to further examinations

This seems to be a weak link of the glaucoma screening procedure as in glaucoma screenings where the glaucoma suspects are to apply to an ophthal mologist on their own initiative further examinations have been found difficult to carry through (*Wolpaw & Sherman* 1954 *Reed & Bendor Samuel* 1957 *Vaughan et al* 1957 *Power* 1957 *Lasky et al* 1959 *Mills* 1959 *Gray* 1960 *Bendor Samuel & May* 1960 *Garner & Dressler* 1961 *Taubenhaus* 1961 *Ra dian et al* 1963 *Aehlig* 1965 *McDonald & Johnsos* 1965 *Bjornsson* 1967)

The author arrived at the same result on routine tonometry in an ophthal mological practice This was carried on concurrently with the investigation un der review and showed that one third of the glaucoma suspects had to be sum moned for re examination (*Norskov* to be published)

To attain to an acceptable solution of this problem a careful co ordination *of the primary screening and the further examinations is required* According to the experience gained from the present investigation such a co ordination is only possible by adapting the additional examinations to the individual de sires of the glaucoma suspects supplemented by intensive search for those who fail to appear However a permanent solution on these lines is hardly pos sible without establishing special glaucoma clinics with the consequences such will involve

Though from a theoretical aspect the applanation tonometer is regarded as the most accurate one of the clinically employed tonometers (*Chandler* 1965 *Pollack* 1967) this type was *the tonometer of choice in only few of the screen ings* reported (*Schmidt* 1960 *Harrison & Wolf* 1964 *Perkins* 1965 *Walker & Vodden* 1966 *Wright* 1966 *Hollows & Graham* 1966 *Norskov* 1967b *Bankes et al* 1968)

In most of these investigations the tonometry was carried out by ophthalmo logists which was also the case in the present study but trained technicians may probably very well be entrusted with performing applanation tonometry (*Per kins* 1965 *Rosenthal* 1967 *Pollack* 1967 *Tonkin* 1966)

Further it is possible with adequate assistance to carry through applanation tonometry as a screening at the same rate as indicated for Schiotz weight tono meter namely 20 25 persons per hour (*Leydhecker* 1961 *Pollack* 1968)

An applanation tonometer attached to the slit lamp has the disadvantage however of being expensive in first cost and difficult to transport This may as is evident from the present investigation interfere with an unrestrained ar rangement of routine tonometry

Scandinavian routine tonometries among persons with apparently normal eyes outside the sphere of action of the ophthalmologist

	number	age	screening level (calibration table)	suspects	%	Glaucoma detected (previously unknown)					
						glaucomatous field loss	%	early glaucoma	%	total	%
Koskenoja & Orma (1955) (home for aged)	600	> 64	≧ 25 mm Hg (≦ 3.5/5.5) (1948)	83	13.8	–	–	–	–	15	2.5
Katavisto & Sammalkivi (1964) (non ophthalmological in patients)	5760	≧ 40	≧ 20.5 mm Hg (≦ 4.0/5.5) (1955)	391	6.8	–	–	–	–	24	0.5
Nørskov (1967) (non ophthalmological in patients)	314	≧ 35	≧ 20.5 mm Hg (≦ 4.0/5.5) (1955) ≧ 20 mm Hg appl	12	3.8	1	0.32	1	0.32	2	0.64
Jensen (1968) (non ophthalmological in patients)	1051	> 40	≧ 22 mm Hg (≦ 3.5/5.5) (1955)	34	3.2	–	–	6	0.6	6	0.6
Stromberg (1962) (total population)	7275	≧ 40	> 20.5 mm Hg (< 4.0/5.5) (1955)	325	4.5	11	0.15	–	–	–	–
Bertelsen et al (1965) (industrial workers)	1909 (1108)	> 19 > 40	≧ 20.5 mm Hg (≦ 4.0/5.5) (1955)	144	7.5	3	0.16	12	0.6	15 15	0.8 1.4

and thorough diagnosing there must be a limit to the number of examinations one can permit oneself to offer among other things because irrespective of the issues one might have difficulty in *convincing* the glaucoma suspects that they are not suffering from a rapidly vision endangering disease

There are also more fundamental causes of the great variations regarding the extents of the additional examinations

It is thus very inconvenient that we have no commonly accepted definition of early glaucoma, while at the same time as in the present *investigation* it is necessary to give an exact definition of early glaucoma by choosing definite pressure values and by selected provocative tests

Moreover the provocative tests are neither sufficiently sensitive nor sufficiently specific and in addition great uncertainty prevails as to whether these tests can foretell the chances of developing visual field defects in the *individual* eyes examined

The uncertainty prevailing regarding the definition of early glaucoma and the concept of normality involves that as a result of any routine tonometry we are left with a poorly defined group having pressures within the range of 20 24 mm Hg characterized as borderline cases In the present series *this group* was three times as large as that with an established glaucoma diagnosis

Opinions differ as to the chances that borderline cases may develop into manifest glaucoma. In some of the screenings reported the chance has been considered to be so great that the borderline cases have been included in the calculated glaucoma frequency (e g *Brav & Kirber* 1951 *Packer et al* 1959 *Dunbar & Goldberg* 1960) *Linner & Stromberg* (1964 1967) on the other hand stated that persons with moderate ocular hypertension rarely develop manifest glaucoma

The group constituting the borderline cases is a deserted group within the glaucoma screening procedure These persons *cannot be told that they are quite* normal they are not to be treated but still to be under control The maintenance of the borderline cases must therefore also be considered when the total work to be performed as a result of glaucoma screening is to be evaluated

Among the new detected glaucoma cases disclosed by routine tonometry of persons with apparently normal eyes the form characterized as early glaucoma predominates as also seen in table 5 In the present study glaucomatous visual field defects were present in no more than 0 10 per cent corresponding to one sixth of the new detected glaucoma cases

The great majority of the cases disclosed by glaucoma screening being thus represented by glaucoma with absence of visual field defects it is evident that the prophylactic value of glaucoma screening depends largely on a knowledge of the further fates of these cases

It is remarkable that only two series are available so far which have been thoroughly examined with a view to assessing the further course in relation to

Regarding glaucoma screening among persons who have no contact with an ophthalmologist the primary screening by tonometry is intended to be carried out by the aid of other medical groups or trained technicians while the remaining part of the glaucoma prophylactic contribution rests with the ophthalmologist

The extra work thereby imposed on the ophthalmologist will depend on the number of persons suspected of glaucoma after the primary screening This number will be influenced by various factors such as the composition of the population group chosen systematic tonometer errors technical errors reading errors and the skill of the examiner The choice of screening level will also play a decisive role

Regarding choice of screening level it is however inconvenient that the lower limit of a harmful intra ocular pressure is not known for the individual eye It has therefore been necessary to define an upper normal limit on the basis of a statistical estimate of so called normal series The term ocular hypertension has been chosen for persons whose intra ocular pressure exceeds the mean value plus twice the standard deviation At the same time it has been tried to fix the screening level accordingly by routine tonometry

The trend is towards a lower screening level than previously and consequently an increased number of persons for further examination Thus a number of investigations have been published within recent years where using applanation tonometer and Schiotz weight tonometer a screening level of 20 21 mm Hg has been preferred (*Hunt* 1966 *Pollack* 1968 see also table 5)

The indications of pressure values above the screening level therefore also differ appreciably as seen in table 5 among others

The present investigation gave a frequency of 3 4 per cent for persons aged 40 or older Various other glaucoma screenings among normal population groups gave the result that more than 10 per cent of the persons examined at the primary screening were referable to further examination (Brav & Kirber 1951 *Wolpaw & Sherman* 1954 *Gradle & Downing* 1957 *Horsley et al* 1958 *Bankes et al* 1968)

At any rate to be able to disclose not previously recognized cases of glaucoma a considerable proportion of the persons with apparently normal eyes must be suspected after glaucoma screening

Further glaucoma screening in the normal population has the disadvantage that a group of persons is left to the care of an ophthalmologist who is expected to promptly make a diagnosis of glaucoma or acquit the examined of the suspicion

This practice has in fact been followed in most glaucoma screenings It means however that the grave diagnosis often as in the present investigation is made after a fairly limited number of examinations However even if one seems to have sufficient working capacity and enthusiasm enough for careful

and thorough diagnosing there must be a limit to the number of examinations one can permit oneself to offer among other things because irrespective of the issues one might have difficulty in convincing the glaucoma suspects that they are not suffering from a rapidly vision endangering disease

There are also *more* fundamental causes of the great variations regarding the extents of the additional examinations

It is thus very inconvenient that we have no commonly accepted *definition of* early glaucoma while at the same time as in the present investigation it is necessary to give an exact definition of early glaucoma by choosing definite pressure values and by *selected provocative tests*

Moreover the provocative tests are neither sufficiently sensitive nor sufficiently specific and in addition great uncertainty prevails as to whether these tests can foretell the chances of developing visual field defects in the individual eyes examined

The uncertainty *prevailing regarding the definition of early glaucoma* and the concept of normality involves that as a result of any routine tonometry we are left with a poorly defined group having pressures within the range of 20 24 mm Hg characterized as borderline cases In the present series this group was three times as large as that with an established glaucoma diagnosis

*Opinions differ as to the chances that borderline cases may develop into ma*nifest glaucoma. In some of the screenings reported the chance has been considered to be so great that the borderline cases have been included in the calculated glaucoma frequency (e g *Brav & Kirber* 1951 *Packer et al* 1959 *Dunbar & Goldberg* 1960) *Linner & Stromberg* (1964 1967) on the other hand stated that persons with *moderate ocular hypertension rarely develop manifest* glaucoma

The group constituting the borderline cases is a deserted group within the glaucoma screening procedure These persons cannot be told that they are quite normal they are not to be treated but still to be under control The maintenance of the borderline cases *must therefore also be considered when the total* work to be performed as a result of glaucoma screening is to be evaluated

Among the new detected glaucoma cases disclosed by routine tonometry of persons with apparently normal eyes the form characterized as early glaucoma predominates as also seen in table 5 In the present study glaucomatous visual field defects were present in no more than 0 10 *per cent corresponding to one* sixth of the new detected glaucoma cases

The great majority *of the* cases disclosed by glaucoma screening being thus represented by glaucoma with absence of visual field defects it is evident that the prophylactic value of glaucoma screening depends largely on a knowledge of the further fates of these cases

It is remarkable that only two series are available so far which have been thoroughly examined with a view to *assessing the further* course in relation to

glaucoma screening namely those of *Linner & Strömberg* (1964 1967) and *Leydhecker* (1960 1966)

Unfornunately the conclusions arrived at are not identical Leydhecker is of the opinion that his results bore out the hypothesis that the rise in pressure pre cedes the visual field defects by 15-18 years a course which is a prerequisite of the prophylactic value of glaucoma screening Linner & Strömberg on the other hand hold that glaucoma screening by tonometry is of no value from a glaucoma prophylactic aspect

In assessing the need for routine tonometry of the normal population the chances of contact with the ophthalmologist must also be considered In Den mark the geographical conditions as well as the structure of the health service afford possibilities of contact with an ophthalmologist In this connection it may be mentioned that 10 per cent of the present series of examined donors had consulted an ophthalmologist within a ten year period Further there is reason to point out that six of the 55 donors suspected to have glaucoma in cluding the two with visual field defects also had been traced by a concurrent routine tonometry carried out by the only ophthalmic medical practitioner of Falster

These reflections offer nothing new However in many papers dealing with glaucoma tracing by tonometry the authors concerned have displayed a ten dency towards underestimating the significance of the problems relating to a glaucoma prophylactic contribution based on tonometry The present in vestigation on the other hand has shown that glaucoma tracing examinations of persons with apparently normal eyes carried through on traditional lines may as often demonstrated disclose cases of not previously recognized glau coma in its widest sense in 1 2 per cent of the population over 40 At the same time however the necessity has been stressed of a more critical view regarding employment of tonometry as an aid in the glaucoma prophylactic work This will in particular find expression in the attitude taken towards glaucoma screening outside the ordinary sphere of action of the ophthalmologists

Summary

The present investigation was carried through with a view to tracing glaucoma by means of applanation tonometry among 2031 persons 18 years old or older belonging to the volunteer donor corps of the Island of Falster (86 per cent of the total number of members)

In 55 donors (2 7 per cent) pressure values above the screening level ($\geq$ 20 mm Hg) were recorded

One or more of the following criteria were required to establish the diagno

sis 1 Distinct marginal cupping of the disc (not observed in the present series) 2 Reproducible glaucomatous visual field defects 3 Pressure measurements of 25 mm Hg or higher 4 A rise of 8 mm Hg or higher in response to water provocative test and 5 a rise of 11 mm Hg or higher in response to priscol provocative test

After further examinations – including provocative tests – of the stated 55 donors a diagnosis of glaucoma was evidenced in 0 59 per cent (12 donors, while for donors aged 40 or older the glaucoma frequency constituted 0 96 per cent. It was in no instance a question of glaucoma at a fairly advanced stage only two donors (0 10 per cent) having presented incipient visual field defects

Eight donors or 14 5 per cent of those subjected to further examination were characterized as normal or false positive all control examinations having given values within the normal range for both eyes including intra ocular pressures below 20 mm Hg

The borderline cases constituted 1 7 per cent (35 donors)

Starting from the experience gained from the present investigation various problems are discussed relating to the carrying through of glaucoma screening by means of tonometry It is emphasized that on this basis we may be justified in a more critical view regarding employment of tonometry as an aid in the glaucoma prophylactic work This will in particular find expression in the attitude taken towards glaucoma screening outside the ordinary sphere of action of the ophthalmologists

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GLAUCOMA SCREENING

II A Five-Year Follow-Up Carried Through in Relation to a Glaucoma Screening Among Members of the Volunteer Donor Corps of the Island of Falster (Denmark)

BY

KNUD NORSKOV

Numerous glaucoma screenings using tonometry have been carried through within the past 15 20 years in attempts to add to the effectiveness of the glau coma prophylactic work (*Leydhecker* 1960 *Ourgaud & Etienne* 1961 *Posner & Fogland* 1964 *Segal & Skwierczynska* 1967 *Pollack* 1968)

To get conclusive evidence of the prophylactic value of examinations for tracing glaucoma it is however important to know the further course in the cases of persons subjected to glaucoma screening by means of tonometry This is particularly important for the persons who have become suspected after glau coma screening but as a matter of fact also for those characterized as normal after such screening

It is therefore surprising that no more than two fairly large thoroughly examined series are available for assessing the further course in relation to glaucoma screening namely those published by *Leydhecker* (1960 1966) and Linner & Strömberg (1964 1967) with observation periods of 3 and 7 years and $1^3/_4$ and 5 years respectively

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Leydhecker's results support the hypothesis advanced by *Goldmann* (1959) on the basis of Leydhesker's primary tracing among 10 000 persons (1959). According to this the ocular hypertension precedes the visual field defects by 15-18 years. This view was also recently borne out by *Dake* (1967).

Linner & Stromberg on the other hand arrived at a different result regarding the further course in the presence of ocular hypertension. They concluded that tracing of glaucoma by tonometry is of limited value as an aid to singling out persons who must be supposed later to develop manifest glaucoma.

Opinions thus differ considerably regarding the further course in the cases detected by routine tonometry and consequently regarding the prophylactic value of glaucoma screening.

On this background the results will be reported below of a five year follow-up carried through in continuation of the original glaucoma screening by applanation tonometry among members of the volunteer donor corps on the Island of Falster.

The follow-up comprised reexaminations and assessment of the course in the donors whose intra-ocular pressure was measured at 20 mm Hg or higher at the primary screening. In addition the course was assessed in the donors characterized as normal after the primary screening on the basis of data obtained from the case records of the only ophthalmic medical practitioner of Falster.

Present Material

In a previous paper (*Vorskov* 1970) the results are reported of glaucoma screening using applanation tonometry among 2031 members aged 18 or older of the volunteer donor corps of Falster.

In 55 donors (2.7 per cent) an intra-ocular pressure of 20 mm Hg or higher was then recorded. After further examinations a diagnosis of glaucoma (simple) was established in 12 donors while 35 were characterized as borderline cases and 8 as normal.

One or more of the following criteria were required to establish the diagnosis: 1. Distinct marginal cupping of the optic disc (which did not occur). 2. Reproducible visual field defects. 3. Intra-ocular pressures of 25 mm Hg or higher. 4. A rise of 8 mm Hg or higher in response to water provocative test. 5. A rise of 11 mm Hg or higher in response to priscol provocative test. The normal group comprised the donors for whom all further examinations gave values within the normal range in both eyes including measurements below 20 mm Hg.

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GLAUCOMA SCREENING

II A Five-Year Follow-Up Carried Through in Relation to a Glaucoma Screening Among Members of the Volunteer Donor Corps of the Island of Falster (Denmark)

BY

KNUD NORSKOV

Numerous glaucoma screenings using tonometry have been carried through within the past 15 20 years in attempts to add to the effectiveness of the glaucoma prophylactic work (*Leydhecker* 1960 *Ourgaud & Etienne* 1961 *Posner & Fogland* 1964 *Segal & Skwierczynska* 1967 *Pollack* 1968)

To get conclusive evidence of the prophylactic value of examinations for tracing glaucoma it is however important to know the further course in the cases of persons subjected to glaucoma screening by means of tonometry This is particularly important for the persons who have become suspected after glaucoma screening but as a matter of fact also for those characterized as normal after such screening

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Table I

Age and sex distribution, and characterization of 52 donors included in the follow up

Age	glaucoma detected		borderline cases		normales		total	
	males	females	males	females	males	females	males	females
25–34	–	–	2	3	1	–	3	3
35–44	–	1	4	2	1	–	5	3
45–54	5	1	1	6	1	1	7	8
55–64		2	6	3	–	–	8	5
65–74	1	–	–	4	2	2	3	6
≥ 75	–	–	–	1	–	–	–	1
Total	8	4	13	19	5	3	26	26

showed the visual field to be normal in all 52 donors Though repeated attempts were made it was thus impossible to reproduce the visual field defect (baring of the blind spot) noticed previously in two donors (three eyes) though only with object size 2/2000 The observed discrepancy between the visual fields on the two examinations might therefore be due to the patient or the ophthalmologist having difficulty in recording when this object size was used Note however that these two donors were both under treatment during the observation period a fact which may have influenced the appearance of the visual field

Pressure level The pressure level during the observation period was estimated for all 52 donors (104 eyes) on the basis of measurements on the follow up examination supplemented by the measurements carried out by the ophthalmologist in the course of the five year observation period (table 2) 44 donors remained untreated A level of 22 m mHg or higher was recorded for 46 eyes corresponding to 44 2 per cent

Among the 8 treated donors (5 from the glaucoma and 3 from the borderline group) only one obtained a reduction of the pressure to below 20 mm Hg while in 10 eyes the level was 22 mm Hg or higher This evidences the difficulty not infrequently prevailing with regard to obtaining an ideal normalization of the intra ocular pressure in persons with ocular hypertension as pointed out by *Walker* (1976) among others

In table 3 the pressure levels recorded for 44 untreated donors (88 eyes) on the ambulant control examination made in continuation of the screening have been set up against the levels found on the follow up examination after five

A Follow Up of the Donors with an Intra Ocular Pressure of 20 mm Hg or Higher on the Screening

The follow up examinations were carried out within the period from September 1967 to February 1968 Only 52 of the original 55 donors could be subjected to this examination A woman aged 55 had died within the observation period and a man aged 71 failed to appear despite repeated written requests Finally only three of the four donors who had left Falster within the observation period could be subjected to reexamination The fourth a man aged 31 was not examined These three donors who were not subjected to renewed control examination had been characterized as borderline cases

The follow up examination after five years of observation comprised estimation of the central visual acuity ophthalmoscopy visual field measurement and applanation tonometry In compliance with the donor s desire the times of examination were evenly distributed between 8 a m and 8 p m This was one of the reasons why the water provocative test was not repeated

The ocular state of the individual donor was assessed on the basis of the results of these reexaminations supplemented if possible by data available for the donors who had consulted the local ophthalmologist within the observation period

20 donors or 36 per cent had consulted the ophthalmologist within the observation period The number was considerably greater than the 16 per cent who had consulted the ophthalmologist within the group characterized as normal after the primary screening Of the 12 donors who had had a diagnosis of glaucoma established one third failed to appear for control (of the remaining 5 were treated) This is another evidence of the tendency even among glaucoma patients to remain absent from control a factor which must be taken into consideration in assesing the prophylactic value of glaucoma screening (*Muller & Glasenapp* 1952 *Wegener* 1953 *Leydhecker* 1963 *Jonkers* 1969 among others)

The age and sex distribution at the follow up of the 52 donors subjected to this reexamination is seen in table 1 The youngest donor was 25 and the oldest 76 years of age The mean age was 51 6 (50 2 for males and 53 4 for females)

Results

Ophthalmoscopy Ophthalmoscopy revealed no changes in the appearance of the optic disc justifying a modification of the previous characterisation In other words both discs were still to be regarded as normal in 51 donors while one donor had an unchanged glaucoma suspicious optic disc in one eye

Visual field measurement Campimetry using object sizes 2/2000 and 6/2000

Table 1

Age and sex distribution, and characterization of 52 donors included in the follow up

Age	glaucoma detected		borderline cases		normales		total	
	males	females	males	females	males	females	males	females
25–34	–	–	2	3	1	–	3	3
35–44	–	1	4	2	1	–	5	3
45–54	5	1	1	6	1	1	7	8
55–64	2	2	6	3	–	–	8	5
65–74	1	–	–	4	2	2	3	6
≥ 75	–	–	–	1	–	–	–	1
Total	8	4	13	19	5	3	26	26

showed the visual field to be normal in all 52 donors Though repeated attempts were made it was thus impossible to reproduce the visual field defect (baring of the blind spot) noticed previously in two donors (three eyes) though only with object size 2/2000 The observed discrepancy between the visual fields on the two examinations might therefore be due to the patient or the ophthalmologist having difficulty in recording when this object size was used Note however that these two donors were both under treatment during the observation period a fact which may have influenced the appearance of the visual field

Pressure level The pressure level during the observation period was estimated for all 52 donors (104 eyes) on the basis of measurements on the follow up examination supplemented by the measurements carried out by the ophthalmologist in the course of the five year observation period (table 2) 44 donors remained untreated A level of 22 m mHg or higher was recorded for 46 eyes corresponding to 44 2 per cent.

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In table 3 the pressure levels recorded for 44 untreated donors (88 eyes) on the ambulant control examination made in continuation of the screening have been set up against the levels found on the follow up examination after five

Table 2

Pressure levels of 104 eyes (52 donors) during the observation period

	<20 mm Hg	20 21 mm Hg	22 24 mm Hg	≥25 mm Hg	total
No treatment	17	35	29	7	88
+ treatment	1	5	7	3	16
Total	18	40	36	10	104

Table 3

Comparison of the pressure level on primary ambulant control examination with that on five year follow up control examination in 88 eyes of 44 untreated donors

Primary ambulant control examination	follow up control examination			
	<20 mm Hg	20 21 mm Hg	22 24 mm Hg	≥25 mm Hg
< 20 mm Hg	14	7	-	-
20–21 mm Hg	-	23	12	1
22–24 mm Hg	3	5	11	3
≥ 25 mm Hg	-	3	4	2

years In 50 eyes (56 8 per cent) the pressure had remained unchanged In 15 eyes (17 0 per cent) a lower level was recorded at the follow up and in 23 eyes (26 1 per cent) a higher level

As the values compared are based on single measurements which need not have been performed at the same time of the day the conclusions that we may be permitted to draw must necessarily be limited It seems evident however that the pressure had not shifted exclusively to a higher level during the observation period In only one donor was the intra ocular pressure seen to have risen to 25 mm Hg or higher in both eyes while a change from below 20 mm Hg to 25 mm Hg or higher never was recorded

Similar shifts to both higher and lower pressure values in the individual cases have been recorded by *Linner & Stromberg* (1964) as well as by *Leydhecker* (1966) This goes to show that the intra ocular pressure is not to be regarded as

a fixed value but is subjects to variations Consequently repeated pressure measurements may result in altered estimates in several cases

Water provocative test At the primary screening 14 of the 108 eyes subjected to water provocative test (13 0 per cent) responded to this by a rise of 8 mm Hg or higher

As stated above the water provocative test was not repeated

However to evaluate the test we may look at the further course in the ten eyes which had a diagnosis of glaucoma established on a pathological water provocative test alone and which had remained untreated during the observation period No more than three of these eyes showed a change of pressure to 25 mm Hg or higher

Note that at the same time four donors (seven eyes) negative to water provocative test showed a rise of the intra ocular pressure to 25 mm Hg or higher at the follow up

Our main impression of the results achieved is thus that the water provocative test seems to be of limited value as a basis for deciding in which cases the pressure will change during a five year observation period to a level that is harmful to the eye – in the present investigation set arbitrarily at 25 mm Hg

I assessing the course during the observation period seen in relation to the chosen classification in glaucoma cases borderline cases and normals we must bear in mind that a possible modification of the original characterization can be based on a change of the pressure level alone None of the 52 donors followed up had developed ophthalmoscopically visible changes nor visual field changes and as stated above the water provocative test was not repeated In conformity with the previously chosen criteria an intra ocular pressure below 20 mm Hg was characterized as normal while pressures ranging from 20 to 24 mm Hg were regarded as borderline values and 25 mm Hg or higher as glaucomatous levels

Donors with an established diagnosis of glaucoma Table 1 shows the age and sex distribution at the time of the follow up for the 12 donors who had had a diagnosis of glaucoma established (in at least one eye) 4 donors were immediately subjected to antiglaucomatous treatment and one nine months later while 7 received no treatment (4 of them did not even appear for control)

It is seen in table 4 that despite intense antiglaucomatous treatment including strong miotics and diamox only one of the 5 treated donors obtained an ideal normalization i e below 20 mm Hg One donor with a persisting intra ocular pressure of 25 mm Hg or higher despite drug treatment had both eyes subjected to antiglaucomatous operation The table also shows that two thirds of the donors had a pressure level of 22 mm Hg or higher without ophthalmoscopy and visual field measurement having revealed development of glaucomatous changes.

As stated above no follow up record including water provocative test has

Table 4

Pressure level during the observation period in the cases of 12 donors (24 eyes) characterized as glaucoma cases

Pressure level	without treatment	+ treatment	total
< 20 mm Hg	–	1	1
20–21 mm Hg	5	2	7
22–24 mm Hg	6	4	10
≧ 25 mm Hg	3	3	6
Total	14	10	24

been carried through comparable to the previously performed further examinations We therefore had no possibility of establishing the glaucoma diagnosis on the basis of the criteria set up at the follow up examination

Donors characterized as borderline cases The age and sex distribution at the time of the follow up is shown in table 1 for the 32 donors characterized as borderline cases As in other borderline cases no treatment was instituted after the conclusion of the further examinations However at a later stage of the observation period treatment was started of three donors of whom only two presented the criteria chosen in the present study for establishing the diagnosis of glaucoma

In one of these a man aged 57 the pressure level had altered from 22 24 mm Hg to 26 mm Hg as the maximum value measured The other was a woman aged 29 who after 18 months consulted the ophthalmologist – not to have her intra ocular pressure controlled as she had promised – but on account of conjunctival complaints Measurement of the pressure gave 30 mm Hg in both eyes During a subsequent stay in the ophthalmic unit pressure values up to 36 mm Hg were disclosed Treatment with pilocarpine caused this donor such troubles that antiglaucomatous surgical intervention had to be carried through on both eyes

It is seen in table 5 that pressure of 25 mm Hg and higher were recorded for four untreated eyes In conformity with the chosen criteria of glaucoma the diagnosis must thus be regarded as established in both eyes of a woman aged 31 and a man aged 50 In both cases a rise was noticed from 22 24 mm Hg to 26 mm Hg as the maximum value measured

A renewed assessment based on the course during the observation period of the conditions in the donors characterized as borderline cases gave the result that in four of the 32 donors a diagnosis of glaucoma must be regarded as

Table 5

Pressure level during the observation period in the cases of 32 donors (64 eyes) characterized as borderline cases

Pressure level	without treatment	+ treatment	total
< 20 mm Hg	3	–	3
20–21 mm Hg	28	3	31
22–24 mm Hg	23	3	26
≥ 25 mm Hg	4	–	4
Total	58	6	64

established according to the criteria chosen As both ophthalmoscopy and visual field measurement showed normal conditions this altered classification was based solely on a change of the intra ocular pressure which even in three of these amounted to no more than a rise from 22 24 mm Hg to maximally 26 mm Hg recorded

In one donor the characterization was on the given lines to be altered to normal

Donors characterized as normal In table 1 we see the age and sex distribution at the time of the follow up for the eight *donors characterized as normal* In six the pressure level had remained unchanged below 20 mm Hg during the observation period In the remaining two the pressure had risen to 20 21 mm Hg in one eye These were therefore referred to the group of borderline cases according to the criteria employed

B Follow Up of Donors Characterized as Normal on the Primary Screening

Few investigations have been made serving to assess the further fates of the persons characterized as normal after routine tonometry *Linner* & *Strömberg* (1967) carried through a five year follow up of 639 persons born within the period 1895 1905 This number constituted 50 per cent of the persons of this age group whose intra ocular pressures had been measured at 4 0/5 5 Schiotz or lower at the primary screening in 1960 (*Stromberg* 1962) In the majority there was fair agreement between the results of the primary measurements and those of the measurements at the follow up Only 25 (3 9 per cent) had an intra ocular pressure < 4 0/5 5 recorded without any influence on the ophthalmoscopic findings or visual field having been noticed

In this connection there is also reason to mention the Des Moines population

study planned by *Armaly* (1960 1962) Armaly carried through a running pressure control of a population group though this is not to be regarded as a proper glaucoma screening

In a previous study (*Norskov* 1967) the author aimed at getting an impression of the further course in 301 patients who after routine tonometry during stay in hospital were characterized as normal judged from the data available from the case records of the only ophthalmic medical practitioner of Falster None of the patients concerned had had a diagnosis of glaucoma established within the five year observation period

Present Material

On the primary routine tonometry among members of the volunteer donor corps of Falster 1976 out of 2031 donors in 1962 1963 were characterized as normal (*Norskov* 1970)

A series of systematic control examinations for the purpose of assessing the course in this group was impossible to carry through An attempt was made instead to get an impression of the further fates of these by utilizing the data available from the case records of the only ophthalmic medical practitioner of Falster

A review of the case records from September 1967 to February 1968 revealed that within a five year period 307 (16 per cent) of the 1976 donors characterized as normal on the primary screening had consulted the ophthalmologist Women predominated as is frequently seen in an ophthalmological practice (*Jensen* 1963 *Lorentzen* 1966) 22 per cent (151) being women and 12 per cent (156) men Further the fairly old age classes were most richly represented Thus while only 17 donors between the ages of 15 and 24 on the first examination had consulted the ophthalmologist the original age groups of 45 54 and 55 64 were represented by 101 donors (19 per cent) and 43 donors (20 per cent) respectively

The patients were examined in accordance with the causes of their consulting the ophthalmologist Ophthalmoscopy showed normal optic discs in all the cases On the eye examination no point was made of a renewed recording of the intra ocular pressure Therefore as seen in table 6 only 39 per cent (121 donors) had this measured Among donors aged 45 or older the percentage was 47 per cent however Table 6 also shows the age and sex distribution at the time of the follow up for the eight donors who had an intra ocular pressure of 20 mm Hg or higher recorded during the observation period The frequencies of pressures of ≥ 20 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg were 6 6 % 3 3 % (4 donors) and 0 83 % (1 donor) respectively The highest intra ocular pressure recorded was 25 mm Hg

After the examinations comprising ophthalmoscopy visual field measure

Table 6

Age and sex distribution of 121 previously *normal* donors who during the observation period had their intra ocular pressure recorded by the ophthalmologist

age	males	females	total	≥ 20 mm Hg	
				males	females
15–24	–	1	1	–	–
25–34	2	3	5	–	–
35–44	24	21	45	1	–
45–54	26	22	48	2	3
55–64	7	12	19	1	1
≥ 65	–	3	3	–	–
Total	59	62	121	4	4

ment and water provocative test (the latter employed systematically in cases only with a recorded pressure of 22 mm Hg or higher) a diagnosis of glaucoma based on the chosen criteria could be established in the case of one donor a man aged 48 The diagnosis was however based solely on pressures of 25 mm Hg or higher

The data obtained from the only ophthalmic medical practitioner of Falster thus justified a diagnosis of glaucoma in one case though without loss of function within a five year period among the donors characterized as normal on the primary screening We must bear in mind however that positive data were available for 307 donors only of whom no more than 39 per cent had their intra ocular pressure recorded

The found frequency of pressures above the screening level cannot be regarded as representative of the whole donor group because these donors constituted an in a two fold sense selected section of the group The donors concerned were to have consulted the ophthalmologist and he must have felt called upon to measure the intra ocular pressure

These findings indicate however that a renewed pressure measurement after a five year observation period among persons characterized as normal on routine tonometry will disclose another series of pressures above the chosen screening level resulting in reflections regarding the necessity of control measurements and other additional examinations

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After the examinations comprising ophthalmoscopy visual field measure

Table 6

Age and sex distribution of 121 previously normal donors who during the observation period had their intra ocular pressure recorded by the ophthalmologist

age	males	females	total	≥ 20 mm Hg	
				males	females
15–24	–	1	1	–	–
25–34	2	3	5	–	–
35–44	24	21	45	1	–
45–54	26	22	48	2	3
55–64	7	12	19	1	1
≥ 65	–	3	3	–	–
Total	59	62	121	4	4

ment and water provocative test (the latter employed systematically in cases only with a recorded pressure of 22 mm Hg or higher) a diagnosis of glaucoma based on the chosen criteria could be established in the case of one donor a man aged 48 The diagnosis was however based solely on pressures of 25 mm Hg or higher

The data obtained from the *only ophthalmic medical practitioner of* Falster thus justified a diagnosis of glaucoma in one case though without loss of function, within a five year period among the donors characterized as normal on the primary screening We must bear in mind however that positive data were available for 307 donors only of whom no more than 39 per cent had their intra ocular pressure recorded

The found frequency of pressures above the screening level cannot be regarded as representative of the whole donor group because these donors constituted an in a two fold sense selected section of the group The donors concerned were to have consulted the ophthalmologist and he must have felt called upon to measure the intra ocular pressure.

These findings indicate however that a renewed pressure measurement after a five year observation period among persons characterized as normal on routine tonometry will disclose another series of pressures above the chosen screening level resulting in reflections regarding the necessity of control measurements and other additional examinations

Discussion and Conclusion

The object of the present investigation was in the first place to get an impression of the further course in a group with ocular hypertension disclosed by routine tonometry among persons with apparently normal eyes

A five year follow up comprising 52 donors (44 untreated) caught by routine tonometry the majority with pressures within the range of 20 to 25 mm Hg gave the results that no glaucomatous changes had occurred during the observation period neither of the visual field nor on ophthalmoscopy Neither was any definite tendency towards a higher pressure level noticed

To judge from the results of the present study the chance that a group of glaucoma suspects with no pathological changes of visual field or on ophthalmoscopy may develop such defects during a five year observation period must be regarded as fairly small This is in agreement with Linner & Stromberg s experience from follow up examinations after 21 months which disclosed no glaucomatous defects on visual field measurement and ophthalmoscopy On examination after five years of observation changes with regard to visual field ophthalmoscopic findings and pressure level were found in few cases only

This view has also been borne out in more summary statements based on follow up examinations carried through by *Bertelsen et al* (1965) *Fruhauf et al* (1967), *Norskov* (1967) and *Graham* (1968)

As stated previously Leydhecker was of a different opinion regarding the further course in persons caught by glaucoma screening On examination after three years of observation he found visual field defects developing in 32 5 per cent of those whose visual fields had previously been characterized as normal Follow up examination after seven years of one fourth of the original number of glaucoma suspects revealed presence of visual field defects in 60 per cent of those with an intra ocular pressure of 22 mm Hg or higher

In agreement with this *Hildreth & Becker* (1957) in a group of glaucoma suspects detected by routine tonometry in an ophthalmic practice noticed that incipient visual field defects had developed in the course of 6 18 months in 39 per cent (49/69 persons) who originally had had a normal optic disc and visual field

Leydhecker (1967) has pointed out as an explanation of the discrepant views regarding the further course in suspects caught by glaucoma screening that his series comprised pathological cases whereas Linner & Stromberg s series had pressure values at a high physiological level among other things because they had ruled out from their follow up persons with values within the range of $< 4.0/7.5$ Schiotz

In the present investigation however the follow up comprised 94 per cent of the persons characterized as glaucoma suspects after the primary screening 44 per cent of these had pressure values of 22 mm Hg or higher during the ob

servation period while the primary screening had revealed incipient visual field defects in no more than two donors This series thus represents the group predominating in all glaucoma tracing investigations in fact the group which gives occasion to many control examinations which are time wasting to both patient and ophthalmologist and also a strain on the nerves of the patient.

The situation is of course *totally different* for the fairly small group of patients displaying a fully developed (manifest) glaucoma with impaired functions at the glaucoma screening These will have the same advantage of the disclosure of glaucoma as when the diagnosis is made by an ophthalmologist

The classification employed on the primary glaucoma screening in glaucoma cases borderline cases and normals *has been preserved in the present* investigation This is the usual and also necessary procedure in screening However the results of the follow up demonstrate the difficulty of maintaining such a classification It might therefore be more appropriate in agreement with *Holloas & Graham* (1966) to use the term ocular hypertension for the whole *group of glaucoma suspects detected on screening* and *reserve the term* glaucoma for the cases presenting pathological glaucomatous changes on visual field measurement and ophthalmoscopy

To be able to assess the glaucoma prophylatic value of glaucoma screening the further course in the cases with an intra ocular pressure below the screening level *must also be considered No direct comparison can be drawn between* the five year control examinations carried through by Linnér & Strömberg of persons between the ages of 60 and 70 and the present investigation in which the assesment resulted from a retrospective study based on data regarding donors aged over 18 obtained from an ophthalmologist during a five year observation period However in both groups *pressure measurements at a follow up* after five years of observation among persons characterized as normal on the original measurements revealed a new series of intra ocular pressures above the previously chosen screening level None of these rises in pressure were associated with glaucomatous visual field defects or defects seen on ophthalmoscopy

Linner & Stromberg have drawn the conclusion that routine tonometry is of limited value as a means of disclosing the cases liable to develop into manifest glaucoma because the persons whose intra ocular presure reaches a high level in the course of a five year observation period are recruited not only from the group with ocular hypertension but also from the group characterized as normal

The question is however whether the whole glaucoma screening problem is not to be viewed from a *different angle* namely from the relation between the considerable number of persons caught by routine tonometry and the proper incidence of manifest glaucoma in the population

Population examinations using tonometry will be of particular value to

throw some light on this question *Hollows & Graham* (1966) on a screening comprising persons between the ages of 40 and 75 found the incidence of simple glaucoma with associated pathological visual field defects and ophthalmoscopically visible changes to be 0 43 per cent One third had been under ophthalmological control prior to the screening A calculation based on Stromberg s screening of persons aged 40 or older gave an incidence of the same order (*Stromberg* 1962)

By way of comparison it may be mentioned that in a survey on Falster per October 1, 1960 before the commencement of the present series of routine tonometries the number of glaucoma cases diagnosed clinically by the only ophthalmic medical practitioner of the island amounted to 0 30 per cent (61 persons) of the population aged 40 or older (20 601 inhabitants aged 40 or older on Oct 1 1960) Of these 0 23 per cent (48 persons) had simple glaucoma

Among the members of the Falster donor corps aged 40 or older glaucoma had been diagnosed in two donors or 0 16 per cent before the routine tonometry

In other words proper cases of manifest simple glaucoma are actually rarer than the usual statements based on glaucoma screening seem to suggest This fact is a concurrent cause of the considerable difficulties prevailing with regard to getting a univocal estimate of the further course in the ocular hypertensive group disclosed by routine tonometry and thus regarding the assessment of the prophylactic value of glaucoma screening among persons with apparently normal eyes

Finally the conclusion must be drawn that the results of the present investigation lend no support to our expectations regarding the prophylactic value of glaucoma screening but that at the same time continued follow up is desirable

Summary

In the present paper the results are stated of a follow up carried through five years after a glaucoma screening by applanation tonometry of 2031 members of the volunteer donor corps of the Island of Falster After the primary tracing 55 donors were suspected of having glaucoma The diagnosis was established in 12 donors after control examinations and provocative tests on the basis of the criteria chosen while 35 donors were characterized as borderline cases and 8 as normal

A follow up was carried through for 52 donors (between the ages of 25 and

16) the majority with intra ocular pressures ranging from 20 to 25 mm Hg 44 of these donors were untreated

It appeared that no glaucomatous changes were seen to have occurred during the five year observation period with regard to visual field and ophthalmoscopy Neither was a general change towards a higher pressure level observed

An assessment undertaken in relation to the classification in glaucoma cases, borderline cases and normals represented by 12 33 and 8 donors respectively gave the following results

None of the 12 donors with an established diagnosis of glaucoma of whom seven were untreated displayed any visual field defects after a five year observation period and only one slight cupping of the optic disc

In four out of 32 donors characterized as borderline cases the intra ocular pressure rose during the observation period to 25 mm Hg or higher justifying a diagnosis of glaucoma though without loss of function One donor was referable to the normal group after the follow up

Two of the eight donors originally characterized as normal were referable to the group of borderline cases after the follow up

An estimate of the course among the 1976 donors characterized as normal after the primary screening is based exclusively on data available from the only ophthalmic medical practitioner of Falster and comprises no more than 16 per cent of the total numb r Only one donor had a diagnosis of glaucoma established though without loss of function

The results of the present investigation have also disclosed the difficulties with regard to the arbitrary classification of glaucoma suspects usually employed in glaucoma screenings It therefore seems preferable to use the term ocular hypertension for the whole group of glaucoma suspects and reserve the term glaucoma for the cases with loss of function.

Further possible explanations are given of the difficulties prevailing with regard to getting a univocal estimate of the further courses in persons caught by glaucoma screening

Finally the conclusion is drawn that the results of the present investigations lend no support to our expectations concerning the glaucoma prophylactic value of glaucoma screening but that at the same time continued follow up is desirable

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throw some light on this question *Hollows & Graham* (1966) on a screening comprising persons between the ages of 40 and 75 found the incidence of simple glaucoma with associated pathological visual field defects and ophthalmoscopically visible changes to be 0 43 per cent One third had been under ophthalmological control prior to the screening A calculation based on Stromberg s screening of persons aged 40 or older gave an incidence of the same order (*Stromberg* 1962)

By way of comparison it may be mentioned that in a survey on Falster per October 1, 1960 before the commencement of the present series of routine tonometries the number of glaucoma cases diagnosed clinically by the only ophthalmic medical practitioner of the island amounted to 0 30 per cent (61 persons) of the population aged 40 or older (20 601 inhabitants aged 40 or older on Oct 1, 1960) Of these 0 23 per cent (48 persons) had simple glaucoma

Among the members of the Falster donor corps aged 40 or older glaucoma had been diagnosed in two donors or 0 16 per cent before the routine tonometry

In other words proper cases of manifest simple glaucoma are actually rarer than the usual statements based on glaucoma screening seem to suggest This fact is a concurrent cause of the considerable difficulties prevailing with regard to getting a univocal estimate of the further course in the ocular hypertensive group disclosed by routine tonometry and thus regarding the assessment of the prophylactic value of glaucoma screening among persons with apparently normal eyes

Finally the conclusion must be drawn that the results of the present investigation lend no support to our expectations regarding the prophylactic value of glaucoma screening but that at the same time continued follow up is desirable

Summary

In the present paper the results are stated of a follow up carried through five years after a glaucoma screening by applanation tonometry of 2031 members of the volunteer donor corps of the Island of Falster After the primary tracing 55 donors were suspected of having glaucoma The diagnosis was established in 12 donors after control examinations and provocative tests on the basis of the criteria chosen while 35 donors were characterized as borderline cases and 8 as normal

A follow up was carried through for 52 donors (between the ages of 25 and

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Untersuchungsmethode

Der Stammbaum (Fig 1) wurde durch sechs Generationen unter Analyse von 86 Mitgliedern aufgezeichnet, 17 Mitglieder wurden von den Autoren unter Anwendung der Applanationstonometrie sowie Tonographie und Wasserbe lastung untersucht Alle wurde gonioskopiert und ophthalmoskopiert Die Glau komdiagnose wurde nach den von *Tarkkanen* (1962) angegebenen Kriterien ge stellt. Die anamnestichen Daten wurden von einem Mitglied der Familie (III/?7) gesammelt und kontrolliert Dieses Mitglied war der Sohn eines Arztes II/13 mit verifiertem Glaukom Nach Moglichkeit wurde die Diagnose der er krankten Familienmitglieder aus der Kartei des behandelnden Augenartzes kontrolliert Im Ausland wohnhafte Mitglieder wurden von Augenarzten am Wohnort untersucht Die Daten wurden den Autoren zu Verfugung gestellt

Resultate

Der Stammvater der Familie (geboren 1808) war aus der Schweiz ausgewandert und starb im Alter von 57 Jahren Eventuelle Augenkrankenheiten sind nicht bekannt Auch konnte uber eventuelles Glaukom bei I/2 nicht Auskunft erhal ten werden Mitglieder der Familie der Frau I/2 leben heute noch und unter ihnen kommt Glaukom nicht vor Der Stammvater scheint somit die Krankheit in seine Familie eingefuhrt zu haben Die erkrankten Mitglieder in Generation

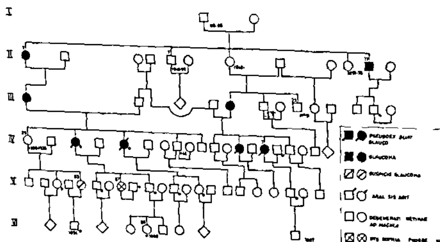


Fig 1

Aus der Universitats Augenklinik Helsinki
(Direktor Professor Salme Vannas)

FAMILIARES VORKOMMEN VON PSEUDOEXFOLIATION UND GLAUKOM

VON

BIRGITTA KNAPE und CHRISTINA RAITTA

Familiares Vorkommen von chronischem Weitwinkelglaukom ist seit langem bekannt Die meisten Arbeiten befassen sich jedoch mit der juvenilen Form des Weitwinkelglaukoms das entweder als ein verspatetes kongenitales Glaukom oder fruhes seniles Glaukom aufgefasst werden kann Die grosse Prevalenz des Simplexglaukoms in der Allgemeinbevolkerung machten das Deuten genetischer Untersuchungen oft schwierig Dominanz Pseudodominanz oder Rezessivitat kann auch nur bei Untersuchung mehrerer als drei nacheinander folgenden Generationen bestimmt werden da sonst die Moglichkeit der Kombination Homozygot und Heterozygot nicht ausgeschlossen werden kann *Tarkkanen* (1962) und spater *Tarkkanen Voipio* & *Koivusalo* (1965) befassten sich mit dem Erbgang bei Pseudoexfoliation und Glaukom In vier Generationen fanden letztgenannte Autoren bei vier Mitgliedern Pseudoexfoliation jedoch nur einmal kombiniert mit Glaukom

Die Verfasser vorliegenden Artikels hatten Gelegenheit eine Familie durch 6 Generationen zu analysieren und Nachuntersuchungen an Mitgliedern 4 Generationen durchzufuhren Es wurde versucht teils den Erbgang festzustellen die zeitliche Reihenfolge Pseudoexfoliation – Drucksteigerung zu evaluieren sowie gleichzeitiges Vorkommen anderer Augenkrankenheiten festzustellen

Eingegangen am 2 September 1969

Untersuchungsmethode

Der *Stammbaum (Fig 1)* wurde durch sechs Generationen unter Analyse von 86 Mitgliedern aufgezeichnet 17 Mitglieder wurden von den Autoren unter Anwendung der Applanationstonometrie sowie Tonographie und Wasserbelastung untersucht Alle wurde gonioskopiert und ophthalmoskopiert Die Glaukomdiagnose wurde nach den von *Tarkkanen (1962)* angegebenen Kriterien gestellt. Die *anamnestischen Daten wurden von einem* Mitglied der Familie (III/?) gesammelt und kontrolliert Dieses Mitglied war der Sohn eines Arztes II/13 mit verifiertem Glaukom Nach Moglichkeit wurde die Diagnose der erkrankten Familienmitglieder aus der Kartei des behandelnden Augenartzes kontrolliert Im Ausland wohnhafte Mitglieder wurden von Augenarzten am *Wohnort untersucht Die Daten wurden den Autoren zu Verfugung gestellt*

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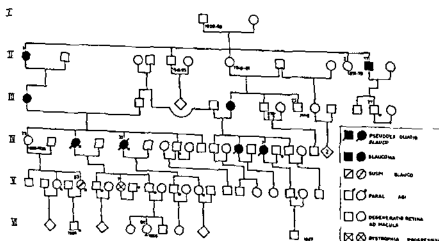


Fig 1

II und III hatten chronisches Glaukom uber Abschilferung der Linsenkapsel sind keine Aufzeichnungen vorhanden Pseudoexfoliation kann nicht ausgeschlossen werden Die Mitglieder IV/31 IV/33, IV/41 und IV/43 haben alle ein Weitwinkelglaukom kombiniert mit Pseudoexfoliation Alle hatten bereits Gesichtsfelddefekte bei dem Stellen der Diagnose Das Alter der Patienten ist heute zwischen 70 und 75 Jahren Das Mitglied IV/29 ist mit 49 Jahren gestorben ohne das ein Glaukom diagnostiziert wurde Ihre Tochten V/53 ist das einzige Mitglied mit suspektem Glaukom und einem Druckniveau das zeitweise 30 mm Hg erreichte Abschilferung der Linsenkapsel wurde bis jetzt nicht beobachtet

Grosse Refraktionsanomalien fehlten in dieser Familie und ausser einer prasenilen und juvelinen Maculadegeneration V/52 VI/80 sowie dem Glaukom und der Pseudoexfoliation lagen keinerlei Augenerkrankungen vor Neurologische Erkrankungen wurden einmal in Form einer Paralysis agitans (VI/33 V/56) und einmal in Form einer Dystrophia musculorum prog-essiva diagnostiziert

Diskussion

Autosomale Dominanz war haufig der Erbgang bei Weitwinkelglaukom *Tarkianen Voipio & Koivusalo* (1965) beschrieben eine Familie in der Pseudoexfoliation ausser mit Myopie und Glaukom auch für sich vorkam

In vorliegender Arbeit scheint sowohl Pseudoexfoliation als auch das Glaukom von einem Gen bestimmt zu sein Das Alter der Patienten bei dem sich die Krankheit manifestierte und der etwa gleichartige Verlauf waren characteristisch Von besonderem Interesse ist das Mitglied V/53 eine Frau mit suspektem Glaukom aber einwandfreier Linse Durch Verfolgen des Verlaufes wird es vielleicht möglich festzustellen ob sich in dieser Familie das Glaukom vor der Pseudoexfoliation manifestiert

In Generation VI ist die Erkrankung wegen des Alters der Patienten noch nicht zu erwarten Es wurde gefolgert dass Pseudoexfoliation und Glaukom in verschiedenen Familien ein variables Vererbungsschema aufweisen kann Es ist somit klinisch wichtig den Typ festzustellen damit man die Fruhdiagnosen stellen kann und auch eine adequate Therapie einrichten kann

Resultate

Ein Stammbaum mit 86 Mitgliedern durch 6 Generationen wurde aufgezeichnet Autosomale Dominanz von Pseudoexfoliation und Glaukom wurde festge

stellt Das Alter der Erkrankten bei dem Manifestieren die Form der Krankheit schien gleichzeitig In keinem Fall wurde Pseudoexfoliation getrennt festgestellt und nur einmal suspektes Glaukom ohne Pseudoexfoliation

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RECOGNITION OF THE LANDOLT RING AS A FUNCTION OF ITS ORIENTATION

BY

VIGO HEMMERSHØJ NIELSEN

Introduction

Differences in visual acuity as a function of different orientations of the test objects have been reported Somewhat similar test objects were utilized in these investigations Higgins & Stults (1 2) in 1948 and 1950 (parallel lines) Leibowitz (3) in 1953 (grating) Ogilvie & Taylor (4) in 1958 (fine wires) and Taylor (5) in 1963 (fine wires) All of the investigations show that a horizontal and vertical orientation of the test object yields a lower detection or recognition threshold than any other orientation In all the studies the threshold for the horizontal and the vertical orientation are approximately identical

Prince & Fry (6) (1958) have studied the problem of the orientation of the test object by using the Landolt Ring Two emmetropic subjects were tested through a 3 millimeter artificial pupil and blurred by a + 1 50 Diopter sphere Their results point towards response differences between the four orientations and they present a formula which proposes to compensate for such response biases

Procedure

Subsequent analysis of the data from a study by Nielsen (7) contains information about the recognition of a Landolt Ring as a function of four orientations

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The experimental conditions were identical for the four orientations and are summarized grossly* in the following points

a) Black test object on white background (contrast ratio approaching + 1 0)
b) Large surrounding field
c) Test field and surrounding field matched in brightness
d) Uniform surface brightness (240 foot lambert)
e) Exposure time of one second
f) Monocular viewing
g) Six observers and 2168 presentations

The experimental procedure was a four alternatives forced choice procedure and the Landolt Rings were presented in random order with the gaps oriented up down right and left Each response was recorded as either right or wrong The threshold was chosen to be at the 62½ per cent correct response level

Results

A frequency distribution of the visual angle thresholds for all orientations for the six observers is presented in Fig 1

Visual angle thresholds for each observer and each orientation is presented in the following table

Table I
Visual angle thresholds for each observer and averages for each orientation (visual angle of the outer diameter of the Landolt Ring)

	Up	Down	Right	Left	X̄
I B	1 66	1 40	1 78	1 91	1 76
B F	1 89	1 72	2.37	2 26	2 06
M O	1 73	2 08	1 95	2.24	2 00
D S	1 96	2 05	1 81	2 08	1 98
F S	1 78	1 84	1 47	1 65	1 69
H T	1 96	2 19	1 87	1 98	2 00
X̄	1 83	1 93	1 88	2 02	1 92

* A more elaborate description of the apparatus and procedure can be obtained from the author s M S thesis Indiana University Bloomington, Indiana USA May 1968

The overall average visual angle threshold of the Landolt Ring (outer diameter) is 1 92 minutes of arc or 0 384 minutes of arc for the gap of the Landolt Ring This is 23 seconds of arc which is in close agreement with Shlaer (8) (22 seconds of arc) and Schober (9) (24 5 seconds of arc)

A statistical analysis of variance was carried out to test a possible difference between the average visual angle thresholds of the four orientations but no statistical difference between them was found A Chi Square test of variance was carried out for each observer to test individual differences but no statistical difference between the four orientations was found for any of the six observers

Discussion and Conclusion

The frequency distribution of visual angle thresholds which is presented in Fig 1 resembles the expected form of a psychometric response distribution Replotted as per cent correct response as a function of increments in visual angle it resembles the familiar S shaped threshold curve

The up" and right" orientations of the gap of the Landolt Ring yield average visual angle thresholds which are slightly lower than the overall average and the down and left" orientations yield thresholds which are slightly higher However the average visual angle threshold for any of the four orientations is within 0 1 minute of arc of the overal average

The results of this study seem best interpreted as a confirmation of the findings from the majority of the cited studies Namely that the orientation of an object or critical object detail in the horizontal and vertical meridian yield visual acuity thresholds which within minor differences statistically are the same

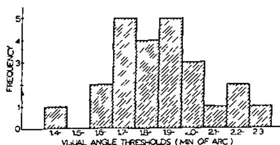


Fig 1

Frequency distribution of the 24 visual angle thresholds based upon the outer diameter of the Landolt Ring

Abstract

nder identical experimental conditions recognition thresholds have been de ermined for four orientations of the Landolt Ring (six observes and 2168 pre entations) The results show that the differences (preferences) between the vi ual angle thresholds of the four orientations for each subject and for the four averages do not differ significantly

Acknowledgment

This study was supported by a grant from *A/S Fisker og Nielsens Fond* Copenhagen Denmark for which the author wishes to express his gratitude

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Dramr ıcn Vorᴌay

60 YEARS RETROSPECT ON GLAUCOMA SIMPLEX

With special reference to Holth s iridencleisis

BY

HARALD G A GJESSING†

The author has passed through his case reports of all his 71 550 patients since he started as an ophthalmologist in Drammen South Norway in 1911 up to the summer 1969 1758 cases of simple glaucoma were found with a total of 26/1 eyes suffering from that disease Only cases of simple glaucoma were included none of the other types e g narrow angle glaucoma glaucoma secundarium

There were three reasons for taking up this examination

I Determination of the frequency of glaucoma simplex

II To give an impression of the course of this disease treated medically or surgically

III To evaluate the results of Holth s iridencleisis at a time when so many other operations are recommended

Many justified objections may arise against such a statement covering so long a period Neither can in a private practice so many examinations be per formed as in the eye departments with their equipment and assistance Many simplifications have been necessary in the daily work for instance the water drinking test has only been used when the coffee test was questionable On the other hand all examinations and operations were performed by the same one man and evaluated by him

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Frequency

In the author s practice simple glaucoma occurred in 2 4 % Ahlström mention ed 2 % among 73 000 patients Malling and Thomas en estimated a percentage of 8 4 based on a material in the University Eye Clinic of Oslo

1058 of the patients were males only 700 females In this the author s ma terial differs from most others

In most of the 1758 cases the disease was monocular when first discovered During the observation period alltogether 2671 eyes were found suffering from simple glaucoma The interval between the two eyes as a rule was several months to a few years

The course of simple glaucoma

For medical treatment was used pilocarpine 2 4 % alone or with addition of eserine 0 5 1 % With exception of Diamox administered systemically other drugs were seldom prescribed Mintacol was used in some few cases but never Phospholine jodide owing to the publications of Uno Axelsson and Per Riise of cataract induced by these drops

It appears that in 1405 cases the medical treatment kept the tension normal In 1?1? the field of vision was found preserved by the last examination but shrunk more or less in 546 cases Visual acuity went down in 408 cases but the decline was seldom more than two lines of the usual Snellen test types

If we take the results by percentage of the three factors in glaucoma tension field of vision and visual acuity it appears that in about 80 % the miotics had a good effect At least they could for a longer period delay the progression of the glaucoma

As the relevant indication for surgical intervention the author has always considered reduction of the field of vision in spite of medical treatment Prior to surgery medical treatment was used in an average of 50 months ranging from one to 3/2 months Only when the patient at the first visit had shown himself undependable in using drops an operation was performed at once

Early operation might give a better prospect of a lasting result But also lasting amaurosis may follow surgery probably having relationship to an oc currence of the cavities of Schnabel But the author finds it a wise rule not to operate without proved loss of function

The author likes to emphasize that no operation for glaucoma gives an ab solutely certain result even if it appears good immediately after the interven tion This stands equally for the iridencleisis as for the other methods

Holth s iridencleisis operation

The good results obtained by the author s teacher S Holth and his friend the dane C F Bentzen induced the author to try the iridencleisis and since 1912 he has used it as the ordinary method Holth s iridencleisis including meridional iridotomy has since been performed in 381 eyes, iridencleisis with peripheral iridectomy and iris inclusion in 14 eyes Other methods were used in 151 eyes

The operation was performed in Holth s original manner The method was published in London 1939 with illustrations Before that time the author had demonstrated the method in Vienna 1927 and in Birmingham Sheffield Man chester and York 1935 After these demonstrations the procedure was often called the norwegian method"

The results from the 381 performed Holth s iridencleisis operations might be summarized as follows 308 (81 %) normal tension a few needing pilocarpine 227 (60 %) preserved visual field 290 (71 %) preserved visual acuity

Even if some authors claim a higher percentage cured by iridencleisis the author thinks his results fairly good The author s material is characterized by a special long observation time and during this might have developed macular degeneration, cataract and optic atrophy

In this material the age of the patients seems to play a rather significant role The prognosis was particularly bad for the youngest patients – whether treated by miotics or surgically In the group from 60 years of age and upwards the prognosis was increasingly better

Having performed 381 iridencleisis operations with meridional iridotomy and 14 with peripheral iris inclusion the author thinks himself justified to draw conclusions as to the value of the method

One advantage is that Holth s operation gives a relatively thick covering of the fistula scar with a rather small risk of late infection This holds true espe cially in the cases with meridional iridotomy The risk of sympathetic ophthal mia is very small and never occurred in this material

A second advantage is that with a well placed iridotomy a dazzling very seldom appears and also that – opposite to iridotasis – the pupil is not drawn up

A drawback of the iridencleisis is – opposed to the Elliot trephination – that the reduction of the intraocular pressure in about half of the cases is not achieved at once but only after some two to three months During this time miotica are to be used The patients are told to come back for reexamination I am sorry not all have done so

It may be added that the author never has seen hypotony after iridencleisis in his material whereas Christiansson had 11 cases of hypotony in 37 opera tions The Seidel fistulation phenomenon very seldom occurred positive in the author s cases

It must be rather unique that the same eye specialist for nearly sixty years has treated his cases of glaucoma simplex in the same manner in the same place and still does His experiences may be of interest in a time when so many new drugs and operations are proposed

Zusammenfassung

In einer augenartzlichen Praktik mit beinahe sechzigjahriger Tatigkeit befanden sich unter einem Krankengut von 71 550 Patienten 1758 Falle von Glaucoma simplex (2 4 %) 1058 waren Manner und 700 Frauen Insgesamt 2671 Augen waren affiziert In 1405 Fallen konnte medikamentose Behandlung die Tension normalisieren In 1212 blieben die Gesichtsfelder unverandert in 546 Fallen waren sie eingeschrankt 546 antiglaukomatose Operationen wurden ausgefuhrt davon 381 Iridencleisen mit meridionaler Iridotomie nach Holth der vom Verfasser *vorgezogene Eingriff Die Resultate* waren *Normalisierung* der Tension in 81 % Konservierung des Gesichtsfeldes in 60 % und Sehscharfe in 71 % Solange die Gesichtsfelder unverandert blieben warnt der Verf gegen Operation. Kein Fall von sympatischer Augenerkrankung kam vor Die Normalisierung des Augendruckes nach Iridencleisis konnte sich zuweilen mehrere Monate verspaten

Holth s iridencleisis operation

The good results obtained by the author s teacher S Holth and his friend the dane C F Bentzen induced the author to try the iridencleisis and since 1912 he has used it as the ordinary method Holth s iridencleisis including meridional iridotomy has since been performed in 381 eyes iridencleisis with peripheral iridectomy and iris inclusion in 14 eyes Other methods were used in 151 eyes

The operation was performed in Holth s original manner The method was published in London 1939 with illustrations Before that time the author had demonstrated the method in Vienna 1927 and in Birmingham Sheffield Man chester and York 1935 After these demonstrations the procedure was often called the norwegian method"

The results from the 381 performed Holth s iridencleisis operations might be summarized as follows 308 (81 %) normal tension, a few needing pilocarpine 227 (60 %) preserved visual field 290 (71 %) preserved visual acuity

Even if some authors claim a higher percentage cured by iridencleisis the author thinks his results fairly good The author s material is characterized by a special long observation time and during this might have developed macular degeneration cataract and optic atrophy

In this material the age of the patients seems to play a rather significant role The prognosis was particularly bad for the youngest patients – whether treated by miotics or surgically In the group from 60 years of age and upwards the prognosis was increasingly better

Having performed 381 iridencleisis operations with meridional iridotomy and 14 with peripheral iris inclusion the author thinks himself justified to draw conclusions as to the value of the method

One advantage is that Holth s operation gives a relatively thick covering of the fistula scar with a rather small risk of late infection This holds true espe cially in the cases with meridional iridotomy The risk of sympathetic ophthal mia is very small and never occurred in this material

A second advantage is that with a well placed iridotomy a dazzling very seldom appears and also that – opposite to iridotasis – the pupil is not drawn up

A drawback of the iridencleisis is – opposed to the Elliot trephination – that the reduction of the intraocular pressure in about half of the cases is not achieved at once but only after some two to three months During this time miotica are to be used The patients are told to come back for reexamination I am sorry not all have done so

It may be added that the author never has seen hypotony after iridencleisis in his material whereas Christiansson had 11 cases of hypotony in 37 opera tions The Seidel fistulation phenomenon very seldom occurred positive in the author s cases

Method and Material

In most cases ocular tension has been measured with a Schiotz x tonometer Some patients have been measured with a weighted Schoitz tonometer only A small number of patients in whom tension was measured only by means of an applanation tonometer have been omitted from this survey Weighted tonometer readings have been converted in accordance with Schiotz s 1924 calibration scale which we feel corresponds best to his original calibration scale for the x tonometer used for this material According to this scale a reading of 3 5 with a 5 5 g plunger corresponds to an intraocular pressure of 27 5 mm Hg and a scale reading of 5 5 with a 7 5 g plunger to 28.5 mm Hg To establish limits for glaucoma we have taken these readings as being equivalent to the scale reading of x/9 (= 28 mm Hg) on the x tonometer The criteria for glaucoma applied are the same as those stated in our first survey (Acta Ophthal 46 1095 1104) namely an ocular tension of x/9 or more if this can be confirmed by repeated measurements or if other symptoms of glaucoma are detected

Our pseudoexfoliation material included only patients in whom pseudoexfoliation or glaucoma had not previously been observed Out of an original total of 389 patients with unilateral pseudoexfoliation 343 were found suitable for comparison of ocular tension in both eyes namely 114 men and 229 women. Patients with traumatic influences of the eyes sequelae as a result of uveitis swollen cataract or other conditions which could be assumed to have an influence on the ocular tension have been omitted

The frequency of glaucoma among patients in the material was 43 0 % in respect of males (49 out of 114 patients) and 22 7 % in respect of females (52 out of 229) In all these cases glaucoma was found in the eye with pseudoexfoliation 7 men (6 1 %) and 8 women (3 5 %) also had glaucoma in the other eye

Result

Figs 1 and 2 show the relative distribution of ocular tension in eyes with and without pseudoexfoliation The curves show the relative distribution of tensions for the material as a whole i e including the glaucoma cases The higher frequency of glaucoma in the men as opposed to the women is revealed by the fact that the curve representing eyes with pseudoexfoliation is more protracted in respect of the men than that of the women The average figures for ocular tension in eyes without pseudoexfoliation are 20 4 mm Hg (S D = 3 82) and 0 mm Hg (S D = 3 41) for men and women respectively It will be apparent that the dispersion is relatively slight The average figures for tension in

From the Eye Department (Head Oluf Roe M D)
Namdal Hospital Namsos Norway

PSEUDOEXFOLIATION OF THE LENS CAPSULE

III Ocular tension in eyes with pseudoexfoliation

BY

EGILL HANSEN and OLE JAKOB SELLEVOLD

It has been well documented that pseudoexfoliation of the lens capsule frequently occurs in connection with glaucoma Clinical experience has shown that in many cases even in patients who show no signs of glaucoma, there can be a higher level of tension in eyes with pseudoexfoliation than in eyes where no pseudoexfoliation is present *Aasved* (1964) in connexion with his mass examination of elderly persons found that the ocular tension in patients with pseudo exfoliation was on an average 3 mm Hg higher than in the material taken as a whole

In our material from Namdal Hospital (Acta Ophthal *46* 1095 1104) we have been especially interested in comparing the tension in both eyes of patients with unilateral pseudoexfoliation We believe that comparisons of this kind can provide useful information about the nature of the tension in eyes with pseudo exfoliation Possible inaccuracies in the method of measuring employed will presumably apply equally as long as measurements are carried out in pairs and in the same way for both eyes in the same patient Furthermore in the case of patients whom it has been possible to keep under observation over a protracted period of time we have attempted to register variability in the average tension level during the period of observation

This investigation was partly supported by a grant from Dr Nils Helsingen s Foundation for Medical Research at Namdal Hospital
Received October 13th 1969

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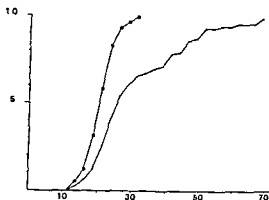


Fig 1

Cumulative polygons showing relative cumulative frequency of ocular tension in 114 men with unilateral pseudoexfoliation The curve on the left shows the distribution of tension for eyes without pseudoexfoliation and the curve on the right that of eyes with pseudoexfoliation The figures along the abscissa indicate the ocular tension in mm Hg and those along the ordinate the relative frequency

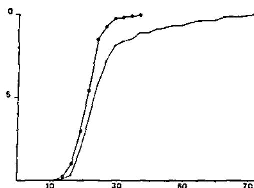


Fig 2

Cumulative polygons showing relative cumulative frequency of ocular tension in 279 women with unilateral pseudoexfoliation Key to signatures as for Fig 1

eyes with pseudoexfoliation is of little interest on account of the many instances of glaucoma in which the tension is considerably increased

By leaving out all the patients with glaucoma we find the distribution of tension shown in Fig 3 The relative distribution of tension for eyes with and without pseudoexfoliation in 65 men and 177 women has been indicated on probability graph paper There is a certain amount of deviation from normal distribution but this is not considerable It will be seen that the tension curves run fairly parallel for both men and women The tension curves in respect of

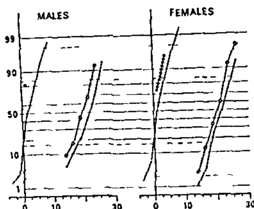


Fig 3

Cumulative polygons showing relative cumulative frequency of ocular tension in 65 men and 1/7 women with unilateral pseudoexfoliation without glaucoma The curves marked with rings indicate the distribution of tension in respect of eyes without pseudoexfoliation while the unbroken lines indicate the distribution of tension in eyes with pseudoexfoliation.

The finely dotted curves show the relative cumulative distribution of deviations in tension between the eye with pseudoexfoliation and that without in the same patient Also shown, for the sake of comparison is the relative cumulative distribution of deviations in tension in respect of the two eyes in 59 men and 88 women with bilateral pseudoexfoliation (square dotted curves)

The figures along the abscissa indicate the ocular tension in mm Hg and those along the ordinate the relative frequency

the women lie closer together which is an indication of a lower average difference in tension in the women than in the men The relative distribution of differences in tension is indicated on the far left of the diagrams The curves which correspond best in the comparison between men and women are those in respect of the exfoliated eyes The average ocular tension for eyes with pseudo exfoliation was 21 38 mm Hg in respect of men (S D = 3 75) and 21 41 mm Hg (S D = 3 ?9) in respect of women and for eyes without pseudoexfoliation 19 ?7 mm Hg (S D = 3 44) and 20 01 mm Hg (S D = 3 15) in respect of men and women respectively

There is thus a marked difference in the level of tension in eyes with pseudo exfoliation compared to those without The greatest difference in tension was 10 mm Hg Also noted in some cases was a lower tension in the eye with pseudoexfoliation than in the other eye 2 of the men (3 0 %) and 11 of the women (6 ? %) had a tension of at least 1 25 mm Hg lower in the eye with pseudo exfoliation than in the eye without On an average however the ocular tension in the eye with pseudoexfoliation was 2 15 mm Hg higher than in the eye

without pseudoexfoliation in the case of men (S D = 2 65) and 1 46 mm Hg higher in the case of women (S D = 2 41) The corresponding t values are 6 56 and 8 04 for men and women respectively in other words the average difference in tension in both cases is significantly greater than 0 (p = 0 01)

Amongst the men 17 out of 65 had a clearly higher ocular tension in the eye with pseudoexfoliation than in the other eye namely a difference of 3 75 mm Hg or more whereas amongst the women 28 out of 177 had a positive difference in tension of 3 75 mm Hg or more in respect of the eye with pseudo exfoliation The difference is not significant (p = 0 05) In other words no real difference can be shown between men and women in respect of the proportion of patients with a clearly higher tension in the eye with pseudoexfoliation

The tension level in eyes with bilateral pseudoexfoliation

Amongst patients with bilateral pseudoexfoliation but without glaucoma in either eye we have made comparisons of the tension levels in both eyes After setting aside all patients with sequelae as a result of uveitis likewise those whose eyes had suffered damage or been subjected to operations or in any way featured conditions which might exercise influence on the ocular tension we were left with 59 men and 88 women in whom the ocular tension in both eyes could be compared Amongst the men the average ocular tension was 19 78 mm Hg (S D = 3 37) and amongst the women 20 94 mm Hg (S D = 3 55) There was an average difference in tension between the eye with the highest tension and the other eye of 0 53 mm Hg in respect of the men (S D = 1 07) and 0 78 mm Hg in respect of the women (S D = 1 42) The results are shown in Fig 3 by means of the square dot curves It will be seen that 81 3 % of the men had a difference in tension of less than 1 25 mm Hg In the case of the women 73 9 % had differences in tension of less than 1 25 mm Hg and 95 5 % had a difference of less than 3 75 mm Hg Thus amongst our patients with bilateral pseudoexfoliation without glaucoma there is very little difference between the level of tension in the two eyes

When comparing the difference in tension in the two eyes in patients with unilateral pseudoexfoliation and in those with bilateral pseudoexfoliation we found that in 30 out of 65 men with unilateral pseudoexfoliation the tension was at least 1 25 mm Hg higher in the eye with pseudoexfoliation than in the other eye Among the men with bilateral pseudoexfoliation only 19 out of 59 showed a difference of at least 1 25 mm Hg between the eye with the highest tension and that with the lowest The difference is very significant (p = 0 01)

As regards the women with unilateral pseudoexfoliation 82 out of 177 revealed a difference in tension of 1 25 mm Hg or more between the eye with pseudoexfoliation and that without whereas only 23 out of 88 in the group with bilateral pseudoexfoliation had a difference of tension of a least 1 25 mm

Hg between the two eyes The difference is very significant (p = 0 01) Furthermore, 28 out of the group of 177 women had a positively higher tension in the eye with pseudoexfoliation of at least 3 75 mm Hg whereas only 4 of the women in the group of 88 with bilateral pseudoexfoliation had such a marked difference in tension between the two eyes The difference is significant (p = 0 05)

Stability of the tension level during the period of observation

In order to determine whether the level of tension in eyes with pseudoexfoliation remains constant or whether there is a tendency for the tension to increase with time we kept a number of patients with pseudoexfoliation in one eye under observation and recorded the variations in tension in this eye from year to year This group comprises patients who did not develop glaucoma and to whom moreover no glaucoma medication was administered

Deviations from the initial tension were noted for each year of observation In the case of patients in whom tension was measured several times in the course of a single year the deviation figure has been assessed as an average of these By initial tension we mean the tension measured the first time pseudoexfoliation was observed in the patient in question Table I shows the results in respect of 36 men and 73 women The average initial tension in the men was 20 3 mm Hg (S D = 3 75) and in the women 20 7 mm Hg (S D = 2 97) The table indicates the average deviation from the initial tension for each year on the basis of the deviations registered for each individual patient It will be seen that the deviations on an average are small over the period of observation as a whole The degree of dispersion however is comparatively large as is revealed by the standard deviations Thus no increase can be demonstrated in the average level of tension in eyes with pseudoexfoliation in these patients who have been kept under observation without developing glaucoma.

Comments

When pseudoexfoliation is first detected glaucoma is also observed in a considerable number of patients In our total material of 736 patients in whom pseudoexfoliation had been recently discovered 45 5 % of the men and 30 8 % of the women had glaucoma (Acta Ophthal 46 1095 1104) Amongst patients who do not have glaucoma when pseudoexfoliation is first detected a number contract glaucoma in due course At least 12 to 14 % of the patients with unilateral pseudoexfoliation developed glaucoma in the course of a 5 year period

Table I

Variations in the ocular tension in patients with unilateral pseudoexfoliation The figures indicate the average deviations from the initial tension calculated on the basis of observations recorded in respect of each individual patient The table refers to eyes with pseudoexfoliation

Year of observation	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	> 10
Males											
No of patients	20	17	10	8	7	7	3	3	1	3	
Average deviation from initial tension	+ 0 5	— 0 5	+ 0 8	— 0 4	— 0 2	+ 0 3	0	— 1 7	0	— 0 3	
S D	2 85	2 61	4 13	3 33	3 34	3 81	3 00	1 53		3 51	
Females											
No of patients	30	34	29	22	18	12	7	5	3	3	3
Average deviation from initial tension	+ 0 5	— 1 1	— 0 3	+ 0 1	— 0 8	+ 0 3	— 0 9	— 0 3	— 3 2	— 3 2	— 2 3
S D	3 38	3 01	3 16	3 02	2 63	4 60	2 46	3 12	4 91	1 89	5 51

of observation whereas on the other hand at least 37 to 38 % were observed during the same period without developing glaucoma (Acta Ophthal 47 161-173) In other words in patients in whom pseudoexfoliation has been recently detected and glaucoma is not present from the outset the chances of developing glaucoma later on are not excessively great though they still exist Observation carried out over an even longer period confirms the same thing It is by no means unusual for patients to have had pseudoexfoliation for many years without any demonstrable damage being done to the eye In such cases the condition appears to become stabilized

In patients examined in the course of the present survey we find when conditions in the two eyes are comparable and glaucoma is not present that the average level of tension is significantly higher in the eyes with pseudoexfoliation compared with the level of tension in eyes in which pseudoexfoliation is not present In the patients with unilateral pseudoexfoliation who were kept under observation without developing glaucoma the tension in the eyes with pseudoexfoliation showed no tendency to increase even after a number of years The tension in these eyes remained astonishingly constant (Table I) A likely explanation is that the essential changes which take place in connexion with pseudoexfoliation occur at an early stage Both the pathological increases in tension which result in glaucoma as well as the small increases in the tension level we have been able to trace in the remaining patients in our material may be assumed to arise during this early phase of the exfoliation process The exfoliation process would appear to be active within a limited period of time only after which it seems to calm down Thus what can be observed later on may therefore to some extent be regarded as a sequela of a process which has already taken place and which in the main has been concluded

Summary

In material comprising 65 men and 177 women with unilateral pseudoexfoliation and otherwise normal eyes a significantly higher level of tension was found in eyes with pseudoexfoliation compared with those in which this condition was not present The average difference in tension was 2 15 mm Hg in the men and 1 46 mm Hg in the women When comparing a group of patients 59 men and 88 women with bilateral pseudoexfoliation but otherwise normal eyes we found that the average difference in tension between the two eyes was much less There were significantly more patients with unilateral pseudoexfoliation in whom tension in the eye with pseudoexfoliation was clearly higher than in the other eye than there were patients in the group with bilateral pseudoexfo

liation in whom a clear difference in tension between the two eyes was observed

In a group of patients with unilateral pseudoexfoliation who had not developed glaucoma during the period of observation a record was kept of deviations in the ocular tension over a number of years No tendency for the ocular tension to increase in eyes with pseudoexfoliation was observed Our findings indicate that the essential changes which affect ocular tension take place during an early phase of the exfoliation process

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Reprint requests to the
Department of Ophthalmology Rikshospitalet Oslo 1 (Dr Hansen)

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Department of Ophthalmology University Hospital and Department of Physiological Chemistry Chemical Center University of Lund Lund Sweden

THE IMPORTANCE OF THE POLYSACCHARIDES FOR THE NORMAL FUNCTION OF THE CORNEAL STROMA

BY

A ANSETH and L. A FRANSSON

A connective tissue consists of cells fibroblasts and a varying number of fibrillar elements collagen and elastin The cells and fibrils are imbedded in an abundant ground substance where the polysaccharides or glycosaminoglycans are the most prominent components The polysaccharides exert many functions Because of their gel properties they prevent spreading of particles and substances in the tissue Their water binding capacity is partly responsible for the fluid balance of the tissue The polysaccharides are negatively charged and therefore link together the fibrillar elements in the tissue and to some extent determine the orientation of newly produced fibrils

The corneal stroma is a specialized type of connective tissue It contains relatively few cells keratocytes which are surrounded by tightly packed collagen fibrils The fibrils generally have a small and uniform diameter and are oriented in lamellas parallell to the corneal surface The polysaccharide content of corneal stroma is 4 4 5 % of the dry weight Approximately two thirds of the stromal polysaccharides consist of keratan sulfate. This polysaccharide is quite characteristic for the cornea as it is only found in relatively small amounts in a few other tissues in the body The remaining one third is chondroitin 4 sulfate (*Anseth* & *Laurent* 1961 *Laurent* & *Anseth* 1961 *Fransson* & *Anseth* 1967) The regular structure of the corneal stroma is the anatomical basis for the transparency of the tissue its most important biological property The transparency of the corneal stroma also depends on its water content Nor

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mally the tissue is in a state of relative dehydration depending on an active transport of water and ions across the endothelial cell layer Thus a balance is maintained between this fluid transport and the osmotic pressure exerted by the macromolecules in the ground substance (*Pirie & v Heyningen* 1956)

Several inflammatory processes and injuries affecting the cornea diminish the endothelial pump" activity resulting in a pathological swelling of the stroma which reduces the visual acuity In less severe cases the edema may disappear completely and normal transparency may return In more severe cases permanent damage to the endothelial cells may cause a chronic edema of the stroma in which non transparent scar tissue is eventually produced

If a correlation exists between the polysaccharide pattern and the optical properties of the corneal stroma changes in the composition of these substances would be expected during transient and permanent reduction of the stromal transparency It is the purpose of this communication to present some experimental data which indicate that the above mentioned correlation really exists Details concerning experimental data and materials and methods used are found in the original papers referred to in the text

Experimental data

1 During the embryonic development in chicken an increase in corneal transparency has been demonstrated (*Coulombre & Coulombre* 1961) This is the result of a simultaneous decrease in the water content of the tissue During the same period of time an increase in the polysaccharide content of the corneal stroma was found (*Anseth* 1961) The most striking increase occured in a polysaccharide fraction containing highly sulfated keratan sulfate with a high molecular weight (eluted with 2 0 M Cl^-) (Fig 1) The rise in transparency and the increase in the above mentioned keratan sulfate fraction are closely related indicating a correlation between keratan sulfate and corneal transparency

2 The stromal edema which appears in connection with pathological conditions afflicting the cornea has been imitated experimentally in rabbits A transient edema is produced by a careful removal of the endothelial cell layer a permanent edema by removal of both the endothelium and the Descemet s membrane In both cases a marked edema appears within a few hours of the operation If only the endothelial cells are scraped off the edema slowly disappears after some weeks or months starting in the periphery of the cornea When the inner surface of the cornea is covered by functioning cells the stroma is again transparent and free of edema The loss of Descemet s membrane seems to prevent the cells from growing in and in these cases a permanent edema of the corneal stroma is created in which non transparent scar tissue appears

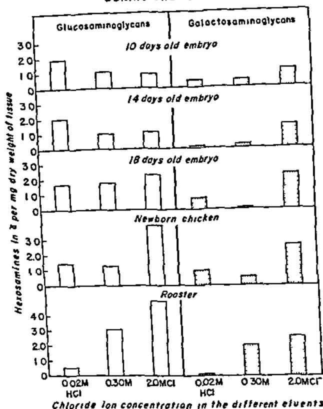


Fig 1

Distribution of polysaccharides from developing chicken corneas in ECTEOLA fractions (glucosaminoglycans = keratan sulfate galactosaminoglycans = chondroitin sulfate)

Analyses of the polysaccharide composition in these corneas at different times after surgery were performed (*Anseth* 1969a, *Anseth & Fransson* 1969) Fig ? shows the changes in the *polysaccharide content during a transient stromal edema* Both the keratan sulfate and the chondroitin 4 sulfate content is reduced to approximately 50 per cent of their original values This is a true loss of polysaccharides and not only a dilution effect because of the increasing water content of the tissue since the values are expressed as hexosamines per dry weight tissue When the edema disappears the polysaccharide content increases again and 3 months after surgery when the edema has disappeared and the cornea has regained its transparency both polysaccharide fractions are normalized No qualitative changes in the polysaccharides have taken place

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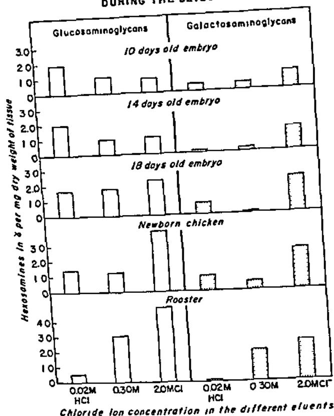


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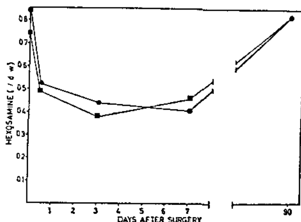


Fig 2
Polysaccharide content in various stages of transient stromal edema
Keratan sulfate ●——●
Chondroitin sulfate ■——■

during the period of edema since the elution pattern seems to be unchanged through the experiment (Fig 3)

The same loss of polysaccharides was found in edematous scar tissue produced by removal of endothelium and Descemet s membrane (Fig 4) In these corneas a chondroitin sulfate like polysaccharide was isolated and the analyses showed that it was dermatan sulfate a polysaccharide normally *not* present in the cornea (*Anseth & Fransson* 1969) Fig 5 shows chromatograms of polysaccharides from normal cornea and from corneal scar tissue 4 and 7 weeks after surgery A gradual accumulation of material eluted with an increasing ion strength is demonstrated in the scar tissue This behavior is typical of dermatan sulfate

Electron microscopy of corneal scars has shown that in this tissue normal corneal fibrils are replaced by coarse fibrils with a greater variety of diameter (*Schwartz* 1953 *Jakus* 1962) It is of interest to note that dermatan sulfate generally occurs in tissues containing coarse collagen fibrils cf skin tendons sclera vessel walls etc (*Meyer Davidson Linker & Hoffman* 1956) Although very little is known about the interactions between polysaccharides and collagen *in vivo* it may be suggested that the presence of dermatan sulfate in the ground substance favors the formation of collagen fibrils with varying fiber diameter (*Jackson & Bentley* 1968)

The results referred to above indicate a correlation between corneal transparency and the polysaccharide pattern of the stroma A transient loss of transparency caused by edema is correlated to quantitative changes in the polysaccharides When a permanent loss of transparency caused by scar tissue for

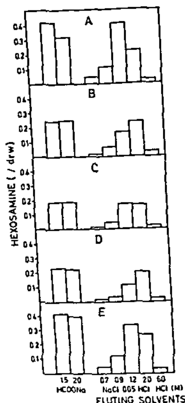


Fig 3

Analyses of normal cornea and edematous cornea at various stages by ECTEOLA formate microcolumn technique

A normal cornea B 12 hr edema C 3 day edema D 7 day edema E 90 days after surgery (healed)

The formate fractions corresponds to chondroitin 4 sulfate and a small amount of low sulfated keratan sulfate while the NaCl fractions contain keratan sulfate

mation develops a polysaccharide is produced which is normally not present in the cornea

It would be of interest to investigate if the changes in the polysaccharide pattern referred to above also takes place in human corneas suffering from different disorders For that reason corneal tissue obtained from the kerato plasty activity at the University Eye Clinic in Lund was divided in 4 diffe rent pools (*Inseth* 1969b)

1 *keratoconus* without edema and scar formation

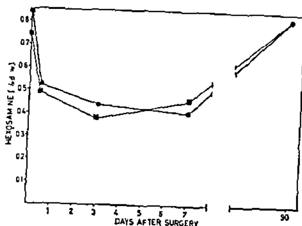


Fig 2
Polysaccharide content in various stages of transient stromal edema
Keratan sulfate ●—●
Chondroitin sulfate ■—■

during the period of edema since the elution pattern seems to be unchanged through the experiment (*Fig 3*)

The same loss of polysaccharides was found in edematous scar tissue produced by removal of endothelium and Descemet s membrane (*Fig 4*) *In these* corneas a chondroitin sulfate like *polysaccharide was isolated* and the analyses *showed that* it was dermatan sulfate a polysaccharide normally *not* present in the cornea (*Anseth & Fransson* 1969) Fig 5 shows chromatograms of polysaccharides from normal cornea and from corneal scar tissue 4 and 7 weeks after surgery A gradual accumulation of material eluted with *an increasing ion* strength is demonstrated in the scar tissue *This behavior* is typical of dermatan sulfate

Electron microscopy of corneal scars has shown that in this tissue normal corneal fibrils are replaced by coarse fibrils with a greater variety of diameter (*Schwartz* 1953 *Jakus* 1962) It is of interest to note that *dermatan sulfate* generally occurs in tissues containing coarse *collagen fibrils* of skin tendons sclera vessel walls etc (*Meyer Davidson Linker & Hoffman* 1956) Although very little is known about the interactions between polysaccharides and collagen *in vivo* it may be suggested that the presence of dermatan sulfate in the ground substance favors the formation of collagen fibrils with varying fiber diameter (*Jackson & Bentley* 1968)

The results referred to above indicate a correlation between corneal transparency and the polysaccharide pattern of the stroma A transient loss of transparency caused by edema is correlated to quantitative changes in the polysaccharides When a permanent loss of transparency caused by scar tissue for

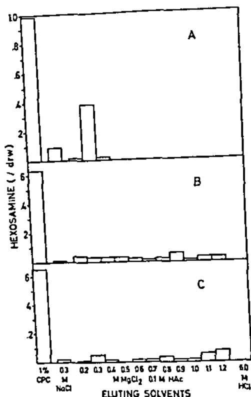


Fig 5

Analyses of normal cornea (A) and corneal scar tissue 4 weeks (B) and 7 weeks after surgery (C) using the CPC cellulose microcolumn technique

These results are in agreement with the data obtained in the experimental studies. A decrease in the polysaccharide content was found in those human corneas where a reduction in the transparency was due to corneal edema and scar tissue formation Dermatan sulfate was demonstrated in corneal disorders where an active scar tissue formation could be expected namely in keratitis and lattice degeneration In keratoconus the decrease in visual acuity is due to the pathological thinning of the cornea and its change of curvature and not to a reduction in the transparency of the tissue. In these corneas no quantitative or qualitative changes in the polysaccharide pattern could be demonstrated

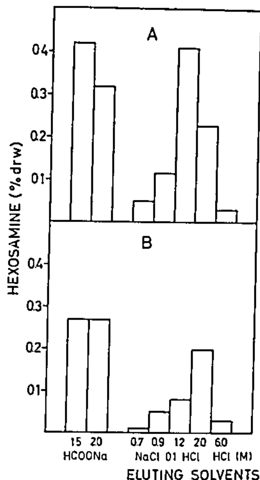


Fig 4

Analyses of normal cornea (A) and corneal scar tissue 6 7 weeks after surgery (B) by the ECTEOLA formate microcolumn technique

2 *keratitis* in an active phase with pathological edema and scar formation

3 *maculae corneae* representing a healed stage of keratitis without edema and

4 *lattice degeneration* in a realtively late stadium of the disease with pathological edema

Fig 6 shows chromatograms of polysaccharides from these four corneal disorders compared with normal human cornea No pathological changes in the polysaccharide pattern was found in keratoconus whereas in the three others a decrease in the polysaccharide content especially in the keratan sulfate fractions could be demonstrated

Dermatan sulfate was found in keratitis and lattice degeneration (Fig 7)

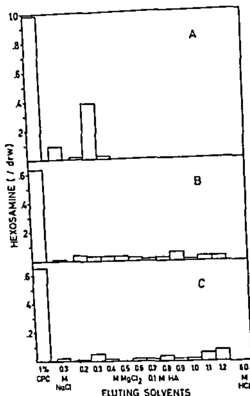


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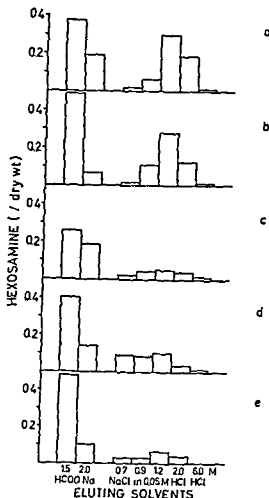


Fig 6

Analyses of normal and pathological human corneal tissue by the ECTEOLA formate microcolumn technique

a normal cornea b keratoconus c keratitis d maculae corneae e lattice degeneration

Summary

Experimental data indicating a correlation between the polysaccharide pattern and the optical properties of the corneal stroma are presented During the embryonic development there is a close relationship between the rise in transparency and the increase in keratan sulfate of the corneal stroma A transient loss of transparency caused by stromal edema is correlated to quantitative changes in the polysaccharides When a permanent loss of transparency caused by scar tissue formation develops dermatan sulfate is produced which is normally not present in the cornea

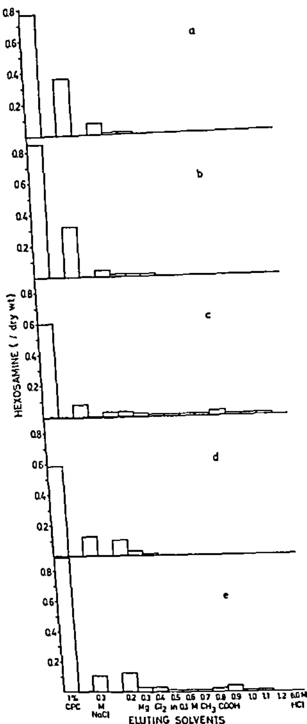


Fig 7

Analyses of normal and pathological human corneal tissue by the CPC-cellulose microcolumn technique

a normal cornea, b keratoconus c keratitis, d maculae corneae e lattice degeneration.

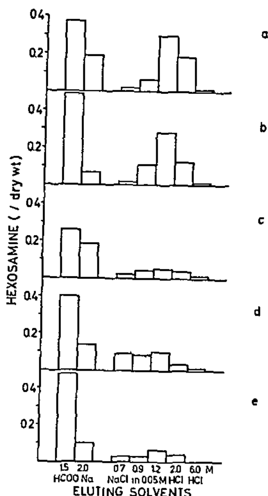


Fig 6

Analyses of normal and pathological human corneal tissue by the ECTEOLA formate microcolumn technique

a normal cornea b keratoconus c keratitis d maculae corneae e lattice degeneration

Summary

Experimental data indicating a correlation between the polysaccharide pattern and the optical properties of the corneal stroma are presented During the embryonic development there is a close relationship between the rise in transparency and the increase in keratan sulfate of the corneal stroma A transient loss of transparency caused by stromal edema is correlated to quantitative changes in the polysaccharides When a permanent loss of transparency caused by scar tissue formation develops dermatan sulfate is produced which is normally not present in the cornea

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ANKYLOBLEPHARON FILIFORME CONGENITUM ASSOCIATED WITH HARELIP AND CLEFT-PALATE

BY

NIELS EHLERS and IB KRARUP JENSEN

Ankyloblepharon filiforme congenitum (or adnatum) indicates a malformation in which the margins of the upper and lower eyelids are connected by extensile tissue bands In the literature 24 cases have been reported

Lohlein (1930) showed a photograph of a baby with ankyloblepharon filiforme and an obvious cleft lip Later this coincidence of malformations have been reported by *Khanna* (1957) and by *Long & Blandford* (1962) *Van der Woude* (1954) described a family with a strong occurrence of labial fistula cleft lip and cleft palate in which one of the patients with labial fistula had unilateral ankyloblepharon filiforme. The present case brings the number of the coincidence of ankyloblepharon and harelip and/or cleft palate up to 5 out of a total of 24 cases of ankyloblepharon filiforme

A total ankyloblepharon in most cases occurs associated with severe facial and ocular malformations *Berndorfer* (1965) in a report of four cases with gross defects of the facial structures presented one with complete cleft lip and cleft palate associated with homolateral total ankyloblepharon and microphthalmos

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The pathogenesis *is not known so far* Inflammation of the lid margins causing defects in the epithelium (*Hasner* 1881 *Mattson* 1950) or traumatic lesions caused by fingernails scratching the epithelium (*Wintersteiner* 1908) have been proposed However no evidence of inflammation in any part of the eye *or its* adnexa has ever been presented in such cases (*Khanna* 1957) Probably an infection would also affect the development of the lashes and glands which have always been found normal Explanation of the condition by trauma is difficult to accept since symmetrical bands in the two eyes may occur

Khanna (1957) considers an anomaly in the separation process To the present authors it seems much more probable in light of the coincidence of ankyloblepharon and harelip and cleft palate that the anomaly is caused by a maldevelopment related in time to the junction of the eyelids and palatine processes and working by mechanisms known from the normal development A possible explanation might be defects in the subepithelial collagen fibres of the eyelids at the time of junction (30 40 mm c r l 8 10 menstrual week)

Summary

A case of ankyloblepharon filiforme congenitum associated with harelip and cleft palate is reported This coincidence of malformations has been observed in 5 out of 24 cases of ankyloblepharon filiforme The possibility of common or related pathogenetic factors is considered

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Case report

A newborn boy was admitted to the University Obstetric Clinic because of lactation difficulties due to complete cleft lip and cleft palate on the right side.

Examination of the eyes showed typical bilateral ankyloblepharon filiforme On the right side the lid margins were connected by a single rather broad strand of tissue while on the left side several delicate strings occupied and partially closed the lateral half of the palpebral fissuere The lids showed no other malformations The eyeballs were of normal size Examinations of the anterior segments and ophthalmoscopy were normal

The ankyloblepharon strands were severed surgically followed by healing without scar formation.

Pregnancy and delivery had been uncomplicated The father and the fathers sister both have harelip and cleft palate while the grandfather was known to have harelip only No other cases of ankyloblepharon are known in the family In the mothers family no malformations are known

Comments

The incidence of harelip and cleft palate is 1 5 per thousand while ankyloblepharon filiforme in extremely seldom The occurrence of harelip and cleft palate in 5 out of 24 cases of ankyloblepharon filiforme suggests common or related pathogenetic factors

The eyelids develop as prominating folds above and below the eye visible already at the 12 mm stage (crown rump length 12 mm) At the 38 40 mm stage the upper and lower eyelids close in front of the eye This junction is purely epithelial mesodermal tissue does not break through the epithelium Before the junction a very thick "basement membrane is seen by light microscopy beneath the junctional epithelium By electron microscopy the thick membrane" is seen as a condensation of collagen and precollagen fibres close to the epithelial basement membrane (*Andersen et al* 1965 1967) Normally the eyelids reopen in the 6th to 7th foetal month

Andersen & Matthiessen (1968) on a human foetal material studied the normal development of the face and made special reference to the development of harelip and cleft palate Comparisons were made with the development of the eyelids During the fusion of the palatine processes no subepithelial condensation of collagen was observed

Microscopy of ankyloblepharon bands have been made several times (*Duke Elder* 1964) and have shown them to consist of a central vascular mesodermal tissue surrounded by squamous epithelium Surgical sectioning of the bands the simple and effective treatment causes bleeding The pathological process in ankyloblepharon filiforme is thus a penetration of the junctional epithelium by mesodermal tissue

results of conventional methods – primarily the capsule forceps – with those of the cataract operations performed by means of cryoextractor

In general where cryosurgery has been used the results of cataract excrations have clearly been considered more successful (*Jensen* 1965 *Rosengren & Enoksson* 1966 *Met* 1967 *Vitali* 1967 *Buschmann & Karrakchou 1968 Dugard 1968 Goldberg* 1968 *Vancea Niculescu & Hagiopol* 1968 *Worthen & Brubaker* 1968 *Seedorff & Lauaet* 1969) For example the number of intracapsular extractions in these materials varies between 82 100 per cent. The capsule rupture of a hypermature cataract also seems to occur easily in the cryoextractions but it is likely to occur even more easily when other methods are used Certain authors have also noticed that results are slightly worse immediately after the employment of the procedure than in a later stage (e g *Rosengren & Enoksson)* According to many authors only the number of intracapsular operations increased with the cryosurgical technique (e g *Worthen & Brubaker*) although some have reported a reduced incidence of vitreous complications (e g *Seedorff & Lauaet*)

The disadvantages of the cryotechnique have naturally been investigated The cryoextractor tip may adhere to the iris cornea or sutures but this has not generally been considered the cause of permanent damage Section should be slightly larger than in capsule forceps extractions – 180 degrees is generally enough to permit application and manipulation of the extractor tip Maximum bending back of the cornea may be necessary it is assumed that excessive manipulation of the cornea and inadvertent cooling/or freezing of the endothelial cells could produce persistent corneal damage (e g *Taylor & Dalburg Jr* 1968) According to several reports corneal complications have not increased and owing to the easier operative course of cryoextractions the operated eye is less apt to develop these reactions (*e g Seedorff & Lauaet*) Criticism has also been made about the overly large size of certain cryoextractors as well as that not all of them stay sufficiently cold for the required length of time

Present study

Material and the operative technique

The material consists of 460 cataracts which were operated on using cryosurgery technique The results of these operations are compared with the control group of 4 0 cataracts in which the lens has been extracted using capsule forceps and alphachymotrypsin In the cryogroup the same enzyme was used in 355 cases (per cent) The number of the male and female cases according to different age and sex groups is presented in Table 1

The cases were largely common senile and mature cataracts The eyes with

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RESULTS OF CRYOEXTRACTIONS OF 460 CATARACTS COMPARED WITH 470 CAPSULE FORCEPS EXTRACTIONS

BY

J A CASTRÉN and J LISTOLA

In 1961 one of the authors made a retrospective study in which results obtained from 470 cataract operations performed by using zonulolysis and an equal number of the same kind of operations without zonulolysis were compared to each other (*Castren* 1961) It was verified then that there were noticeably better results with alphachymotrypsin The following results reveal an especially significant statistical difference

1) The ruptures of the lens capsules decreased in the enzyme group from 21 to 11 per cent

2) Vitreous prolapses during the operation occurred in 13 per cent of the cases but in the group in which the enzyme was not used the corresponding percentage was 23 per cent

3) After the cataract extraction 74 per cent of the enzyme group and 66 per cent of the control group had good vision (0 5 1 6)

4) Four per cent of the enzyme group and eight per cent of the control group had final vision less than F C 1 m or blindness

In the same year that the study mentioned above was printed *Krwawic* published his cryoextraction method Since then many results have been published about materials on which the procedure mentioned was used But there are relatively few studies in which an attempt has been made to compare the

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Table 2
Number of different cataracts

Type of cataract	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
Cataracta senilis hypermatura	8	8	16			
Cataracta senilis matura	133	181	314	76	174	250
Cataracta senilis fere matura	25	25	50	42	62	104
Cataracta complicata	30	26	56	16	37	53
Other cataracts	8	16	24	23	40	63
Total	204	256	460	157	313	470

technique When defrosting was required due to adherence of the tip to the iris cornea or section the other assistant has irrigated this place with warm saline After the delivery of the lens additional Barraquer s silk sutures were used – lately up to six–eight sutures due to the longer section Acetylcholin was injected into the anterior chamber or pilocarpin and eserin were instilled upon the eye The pupil was dilated on the second day – in some cases later after the operation steroid drops were instilled later The triangular silk suture was usually removed 8 12 days after the operation – Since 1966 cryoextraction of cataracts has been in routine use in our clinic The follow up time was from three months to four years

Results

Cryoextraction succeeded intracapsularly 421 times or in 91.5 % of the cases (Table 3) The corresponding figures in the control group were 419 and 89 2 %. The difference however was not statistically significant For those under 40 the capsule ruptured in three cases out of fourteen in the cryo group (21 4 %) and in three out of eleven in the control group (27.3 %)

In reference to complications occurring during the operation the cornea ad

Table 1
Number of cataract operations in different age and sex groups

Age in years	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
0–10	–	–	–	1	–	1
11–40	6	8	14	4	7	11
41–50	17	10	27	12	9	21
51–60	44	38	82	32	38	70
61–65	32	38	70	21	43	64
66–70	34	51	85	25	54	79
71–75	34	43	77	38	73	111
76–80	28	35	63	14	63	77
>80	9	33	42	9	26	35
Total	204	256	460	157	313	470

light perception vision were recorded as having mature cataracts Hyperma turity was a diagnosis only where so stated in the operative notes or records Table 2 shows the different forms of cataracts in the material

Only a few of the operations were performed under general anaesthesia After the usual pre medication (Pentobarbital 50 100 mg Pethidin 50 100 mg often Lergican 50 mg 1 hr b oper) and the facial nerve block (O Brien and/or van Lint) retrobulbar injection was made The bridle suture was passed by the insertion of the sup r muscle 1 0 triangular silk corneoscleral suture was in serted before opening the anterior chamber Flieringa s ring was sutured in highly myopic eyes A relatively short section was made up and then lengthen ed both nasally and temporally with scissors After two peripheral iridotomies two appositional sutures either Barraquer s silk or rat tail suture were placed on both sides of the triangular suture The enzyme was injected behind the iris the ant chamber and the section were irrigated with warm normal saline – In the control group the operator performed the delivery of the lens so that the corneal flap was raised by lifting the triangular suture with the left hand while applying the capsule forceps to the lens capsule with the right hand The assistant pushed gently at 6 o clock with the squint hook In cryoextractions the operator removed the iris by using the pupil margin double retractor while applying the extractor at the same time on the upper part of the lens surface with his right hand The assistant raised the corneal flap and dried the lens surface In each case the delivery of the lens was attempted by the sliding

hered to the cryoextractor nine times (two per cent) and the iris 27 times (5 9 %) Permanent injuries could not be shown in any of these cases

Cases of vitreous loss during the operation totalled 25 or 5 4 per cent in the cryo group but more than the double or 58 (12 6 per cent) in the control group (Table 4) The difference was highly significant

Vitreous prolapses after the operation occurred only twice in both the cryo and the control group (Table 5) Postoperative iris prolapses occurred in the former group 18 times (3 9 per cent) and in the control group only in nine cases (1 9 per cent) This difference however was not statistically significant

The cases of vitreous in the anterior chamber with ruptured anterior hyaloid membrane are presented in Table 6 Such cases occurred in the cryo group 39 times or in 8 5 per cent but in the control group 159 times or in 33 9 per cent. This difference was also highly significant

Table 4

Vitreous loss during the operation Number of the cases

Sex	Control group		Cryo group	
	No loss of vitreous	Vitreous loss	No loss of vitreous	Vitreous loss
Males	191	11	137	20
Females	244	14	275	38
Total	435 (94 5 %)	25 (5.5 %)	412 (87 4 %)	58 (12 6 %)

Table 5

Number of cases with post operative vitreous and iris prolapses

Sex	Cryo group		Control group	
	Vitreous prolapse	Iris prolapse	Vitreous prolapse	Iris prolapse
Males	1	8	1	4
Females	1	10	1	5
Total	2 (0 4 %)	18 (3 9 %)	2 (0 4 %)	9 (1 9 %)

Table 3
Number of intra and extracapsular extractions

Sex	Cryo group			Control group		
	Intra	Extra	Total	Intra	Extra	Total
Males	179 (87 8 %)	25 (12 2 %)	204	132 (84 1 %)	25 (15 9 %)	157
Females	242 (94 5 %)	14 (5 5 %)	256	287 (91 7 %)	26 (8 3 %)	313
Total	421 (91 5 %)	39 (8 5 %)	460	419 (89 2 %)	51 (10 8 %)	470

(10 4 per cent) of the cryo grup and in the control group in 70 cases (14 9 per cent) This difference was not statistically significant.

Post operative secondary glaucoma (Table 8) was detected in the cryo group in 17 eyes (3 7 per cent) and in the control group in 15 eyes (3 2 per cent) This difference was not significant

Late retinal detachments occurred after the cataract operation (Table 8) in the cryo group in ten cases or in 2 2 per cent and in the control group in six cases (1.3 per cent) The difference was not statistically significant.

Vision after cataract operation in this matrial appears in Table 9 Information on visual acuity in four cases is unfortunately lacking These patients either died or were moved after the operation to another hospital Vision of 0 5 1 6 was obtained in 318 eyes (69 7 per cent) in the cryo group and in 345 eyes (74 0 per cent) in the control group This difference was not statistically significant

A very poor result – vision less than F C. 1 m – was the final outcome in 23 cases (5 0 per cent) in the cryo group and in 19 cases (4 1 per cent) in the control group The difference was not significant

Discussion

Since the quantities of the cryo and control material were the same (460 470 cases) and were operated on in the same way with the exception of the extraction itself they are probably comparable Since our clinic is a teaching hospital many different individuals have performed the operations (about 20 in both

Table 8

Number [illegible] cases of secondary glaucoma and retinal detachment after cataract surgery

Sex	Cryo group		Control group	
	Secondary glaucoma	Retinal detachment	Secondary glaucoma	Retinal detachment
Males	9	4	8	5
Females	8	6	7	1
Total	1[illegible] (3 [illegible])	10 (2[illegible])	15 (3 2[illegible])	6 (1.3 [illegible])

Table 6

Number of cases with post operative iritis uveitis and vitreous in the anterior chamber with ruptured ant hyaloid membrane

Sex	Cryo group		Control group	
	Iritis or uveitis	Vitreous in ant chamber	Iritis or uveitis	Vitreous in ant chamber
Males	18	15	12	54
Females	18	24	6	105
Total	36 (7 8 %)	39 (8 5 %)	18 (3 8 %)	159 (33 9 %)

Post operative iritis and uveitis (Table 6) occurred 36 times (7 8 per cent) in the cryo group but in only 18 cases (3 8 per cent) of the control group This difference was significant Iritis and uveitis cases lasting less than three weeks are not included in these figures since a slight irritation of iris is common after cataract operation

Complications of the cornea (keratitis descemetitis oedema and vasculariza tion of the cornea) lasting more than three weeks have been considered in Table 7 In the cryo group such complications occurred 19 times (4 1 per cent) and in the control group in 12 cases (2 6 per cent) However this difference was not statistically significant

Post operative choroidal detachments (Table 7) were ascertained in 48 cases

Table 7

Number of cases with post operative corneal complications and choroidal detachments

Sex	Cryo group		Control group	
	Corneal complications	Choroidal detachments	Corneal complications	Choroidal detachments
Males	7	23	6	28
Females	12	25	6	42
Total	19 (4 1 %)	48 (10 4 %)	12 (2 6 %)	70 (14 9 %)

materials) The first operations of about 16 doctors specializing in ophthalmology are included in the figures for both materials

One of the most common complications in cataract operations is the capsule rupture It has decreased from 10 8 per cent of the control group to 8.5 per cent of the cryo group This complication happened relatively more often with hypermature cataracts or when the cataracts of those under 40 years of age were being removed However in operations on young patients for example capsule ruptures decreased from 2/ 3 per cent to 21 4 per cent.

Perhaps the most vexatious complication in cataract operations vitreous loss was brought down from 12 6 % of the control material to 5 4 % in the cryo group This gratifying result was also highly significant statistically In our opinion this might be due to the fact that it is not necessary to push the lens as much when performing the cryoextraction as when adhering to it with forceps neither is so much counterpressure needed from outside of the eye Seedorff & Lavaetz also verify in the material from cases 2 X 413 that vitreous loss decreased in the cryo group to two per cent from the ten per cent of the forceps erisiphake group

We further verified that post operative hyaloid membrane rupture and vitreous in the anterior chamber occurred in only 8 5 per cent of our cryo x traction group in comparison with 33 9 % in the control group This was a highly significant difference

In the cryo group we had post operative iritis lasting over three weeks in 7 8 % of the cases but in only 3 8 % in the control group The difference was significant It is difficult to determine the cause with certainty but the employment of the iris retractor may provide a clue in this respect The instrument was in the operator s poorer hand and his attention was properly fixed on the lens and the tip of the extractor

Keratitis descemetitis oedema and vascularization of the cornea appeared in 19 cases (4 1 per cent) in the cryo group and 12 cases (2 6 per cent) in the control group The difference was not statistically significant There were no cases in which adherence of the extractor to the cornea could be cited as a cause of omplications Otherwise such adhering occurred in only two per cent of the operations

In the interest of the severe complications of the cornea, six cases operated on during the earlier period of the cryosurgery of cataracts should be presented The preoperative diagnoses were the following

Chronic uveitis with secondary glaucoma in one case three cases were complicated by glaucoma with accompanying endothelial degeneration. The cataract extraction was performed also in an eye having perforating injury and a probable phakoanaphylactic uveitis. In two cases the cornea seemed to be normal before the operation – The age of the patients was between 58 82 years excepting one of 43 years (with corneal perforation)

Table 9

Final vision after cataract operations

Vision	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
0 - F C 1 m	7	16	23 (5 0 %)	8	11	19 (4 1 %)
I C 1 m - F C 5 m	7	15	22	11	14	25
0 1 - 0 4	28	65	93	20	57	77
0 5 - 1 6	158	160	318 (69 7 %)	117	228	345 (74 0 %)
Total	200	256	456	156	310	466

materials) The first operations of about 16 doctors specializing in ophthalmology are included in the figures for both materials

One of the most common complications in cataract operations is the capsule rupture. It has decreased from 10 8 per cent of the control group to 8.5 per cent of the cryo group This complication happened relatively more often with hypermature cataracts or when the cataracts of those under 40 years of age were being removed However in operations on young patients for example capsule ruptures decreased from 27 3 per cent to 21 4 per cent

Perhaps the most vexatious complication in cataract operations vitreous loss was brought down from 12 6 % of the control material to 5 4 % in the cryo group This gratifying result was also highly significant statistically In our opinion this might be due to the fact that it is not necessary to push the lens as much when performing the cryoextraction as when adhering to it with forceps neither is so much counterpressure needed from outside of the eye Seedorff & Lavaetz also verify in the material from cases 2 × 413 that vitreous loss decreased in the cryo group to two per cent from the ten per cent of the forceps erisiphake group

We further verified that post operative hyaloid membrane rupture and vitreous in the anterior chamber occurred in only 8 5 per cent of our cryoextraction group in comparison with 33 9 % in the control group This was a highly significant difference

In the cryo group we had post operative iritis lasting over three weeks in 7 8 % of the cases but in only 3 8 % in the control group The difference was significant It is difficult to determine the cause with certainty but the employment of the iris retractor may provide a clue in this respect The instrument was in the operator s poorer hand and his attention was properly fixed on the lens and the tip of the extractor

Keratitis descemetitis oedema and vascularization of the cornea appeared in 19 cases (4 1 per cent) in the cryo group and 12 cases (2 6 per cent) in the control group The difference was not statistically significant There were no cases in which adherence of the extractor to the cornea could be cited as a cause of complications Otherwise such adhering occurred in only two per cent of the operations

In the interest of the severe complications of the cornea six cases operated on during the earlier period of the cryosurgery of cataracts should be presented The preoperative diagnoses were the following

Chronic uveitis with secondary glaucoma in one case three cases were complicated by glaucoma with accompanying endothelial degeneration. The cataract extraction was performed also in an eye having perforating injury and a probable phakoanaphylactic uveitis In two cases the cornea seemed to be normal before the operation – The age of the patients was between 58 82 years excepting one of 49 years (with corneal perforation)

In all cases the extraction succeeded *intracapsularly alphachymotrypsin was* used but additional silk – up to six apposition sutures in one case – were *needed* – *In all cases the postoperative* course was complicated by a severe uveitis Damage of the endothelium and persistent opacification of the cornea occurred in five patients Epithelial cell growth into the anterior chamber was suspected but ingrowth could be verified histologically after enucleation only in that case with scarred corneal wound due to injury

On the basis of these clinical observations some correlations seem obvious

– The relatively large size of the cryoextractor used in these operations the reduced temperature gradient chemical irritation and the larger section combined with excessive manipulation of the cornea might be influenced hazardously on the metabolism of the cornea of these patients who already had a reduced endothelial function – Additional silk sutures due to a longer section may play a significant role in cases of suspected epithelial elements in the anterior chamber though this could not be confirmed

In general we felt the small number of corneoscleral sutures we have mostly used was the preventive factor explaining the small incidence of epithelial *downgrowth in our clinic (Vannas 1957) Furthermore our most important* suture the preplaced triangle suture of Vannas passed over the wound excluding any suture tracts to lead into the anterior chamber

In relation to choroidal detachments post operative glaucoma late retinal detachments and the final visual acuity of those operated on *statistical* differences did not appear

In conclusion it can be said on the basis of this study that cryoextraction seems to be the safest procedure for cataract operation at the present It is suited for difficult cases but according to our experience on some occasions the risks should be carefully compared with the benefits of this method

Summary

The material *consisted of 930 cases of cataract extraction in* the University Eye Clinic in Helsinki 460 were operated on using cryoextraction (lately extractor model Stahl) and *470 extractions (the control group) were made* using alpha chymotrypsin and capsule forceps In the cryoextraction group zonulolysis was used in 77 per cent of the cases *All 930* operations were *tried to do by means* of the intracapsular method

The operation succeeded intracapsularly in *91 5 per cent of the cryogroup* and in 89 2 per cent in the control group The difference was not statistically significant

The cornea adhered to the cryoextractor nine times (two per cent) and the

iris 2ı times (5 9 per cent) Permanent damage from these complications could not be observed

Vitreous loss during the operation occurred more rarely (5 4 per cent) in the cryo group than in the control group (12 6 per cent) This difference was highly *significant*

Post operative vitreous prolapses occurred in both groups only twice Post operative iris prolapses occurred in 3 9 per cent of the cases in the *cryo group* and in 1 9 per cent of the control group This difference was not significant

Vitreous in the anterior chamber with ruptured anterior hyaloid membrane *occurred only* in 8 5 per cent of the cryo material but in 33 9 per cent in the control group The difference was highly significant

Iritis or uveitis lasting more than three weeks after *the operation* was detected in 7 8 per cent in the cryo group but only in 3 8 per cent in the control group The iris retractor was suspected to be one of the causes of this complication

In relation to corneal complications as well as choroidal detachments secondary glaucoma retinal detachments and the final visual acuity statistical differences were not verified

On the basis of this study cryoextraction is considered the safest procedure for cataract operations for the present The possible causes of corneal complications are considered in details in the discussion

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From the Ophthalmic Department of the University Hospital Turku Finland
(Head Prof Arvo Oksala)

EXPERIMENTAL OBSERVATIONS ON THE REFLECTION AND INTERFERENCE PHENOMENON OF THE ULTRASOUND CAUSED BY ORBITAL FAT AND MUSCULAR TISSUES

BY

ARVO OKSALA and ANJA NIIRANEN

In its refraction and reflection ultrasound follows the same laws as light Under certain circumstances refraction is followed by total reflection When ultra sound passes from one substance into another that has a higher sound velocity the angle of refraction is greater than the angle of incidence When the angle of refraction becomes greater than 90° the results is total reflection The rela tion between the angles of incidence and refraction depends on the velocity of sound in the particular substances

The refraction and reflection of ultrasound in the eye and orbit have been examined very little *Oksala* & *Hakkinen* (1969) have found out that if the ultrasound hits the cornea and sclera at a 70° angle of incidence a total re flection is often observed When the ultrasound meets the surface of the lens at the same angle (70) the result may also be a total reflection (*Oksala* 1969)

In this experimental study we have tried to find out if the fat and muscular tissues of the orbit can reflect ultrasound and how high is the sound pressure in a reflected sound beam At the experiments we observed under certain circum stances a strong increase in sound pressure as compared with control tests and this has been thought to be due to an interference phenomenon or to a focusing effect of the tissues

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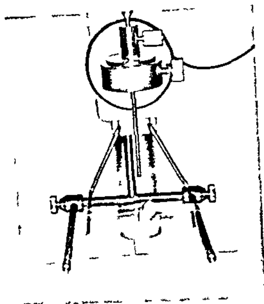


Fig 2

Above one can see a barlike transducer of 7 5 Mc/2 mm and beneath this between the copper wires there is a piece of orbital muscle and further down the steel ball

passed the center of the transducer The intensity of the equipment was kept all the time at the same level (db reserve = 10) which is a level that is often used also in clinical diagnosis

When the transducer is moved one obtains various echo amplitudes which are directly proportionate to the sound pressures at the corresponding points Control curves were obtained when the examination was carried out in water without any tissues

Reflection was studied with 12 different pieces of muscular and fat tissue At these examinations the angle of incidence in relation to the tissue was approximately [illegible]0

The interference and strengthening phenomenon was clearly observable in echo amplitude curves when the angle of incidence was about 60 For these examinations also 1[illegible] different pieces of muscular and fat tissue were used

Results

When the angle of incidence was about [illegible]0 one could always whenever it was wanted produce a total reflection with both muscular and fat tissue As the

Equipment material and research methods

The ultrasonic equipment was Kretztechnik s model 7000 The frequency of the transducer was 7 5 Mc and its diameter 2 mm For the measurement of the sound fields we had constructed an instrument shown in Fig 1 There the transducer is fixed to a stand and beneath the transducer we have a vessel full of water in which a SKF steel ball (diameter 1 5 mm) is moved The position of the steel ball in relation to the transducer can be measured from three directions with a 0 1 mm accuracy Fat and muscular tissues were prepared from the orbits of recently killed pigs The muscular tissue was taken from the outer muscles of the eye Plates of fat tissue were found from the vicinity of eye muscles The thickness of muscular tissue was 4 6 mm and that of fat tissue 2 4 mm

The examination took place in the far field of the transducer the distance of the ball from the transducer being 30 mm Pieces of fat or muscular tissue were fixed between copper wires so that the distance from the transducer to the anterior surface of the tissue was about 15 mm (Fig 2) The copper wires were outside the sound field During the examinations the ball was moved so that it

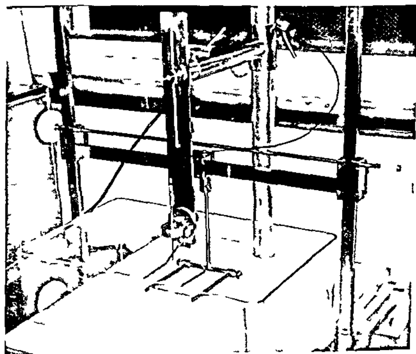


Fig 1

The figure represents an apparatus that has been built for the measurements of sound fields The transducer is fixed to a stand and beneath it there is a vessel filled with water in which a steel ball of 1 5 mm can be moved in three different directions

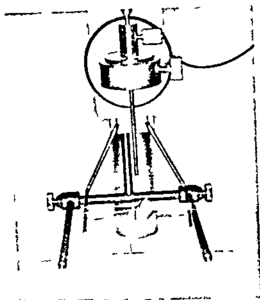


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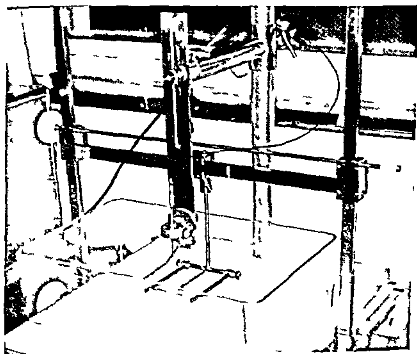


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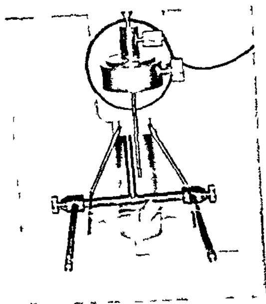


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When the angle of incidence was about ,0 one could always whenever it was wanted produce a total reflection with both muscular and fat tissue As the

examination with the steel ball covers only one cross section of the sound field at a time sometimes the search for the total reflection took a little longer sometimes a little less Finding the total reflection was easier with muscular than with fat tissue Fig 3 shows typical examples of total reflection in muscular and fat tissue The readings of the abscissa denote millimeters and those of the ordinate relative echo amplitudes The curve on the right represents a typical regular echo amplitude curve obtained in water The two echo amplitude curves on the left which consist of a continuous line have originated from a total reflection caused by a muscle while the curves that are made of a discontinuous line have been produced by a total reflection by fat tissue Muscular and fat tissues have reflected the sound beam and at those points of the sound field where measurements have been made one can observe fairly high sound pressures as compared with those of the control curve

Fig 4 represents typical examples of the changes in the sound field caused by muscular and fat tissues when the angle of incidence is approximately 60° On the right we have again a typical control curve obtained in water The curves on the left that are made of a continuous line have been obtained from muscular tissue and the ones with a discontinuous line from fat tissue All measurements gave similar echo amplitude curves We can see that muscular and fat tissues bring forth strong maxima and minima in the echo amplitude curves The maxima may considerably surpass the maximum of the control curve After passing through muscular or fat tissue the sound fields are definitely narrower

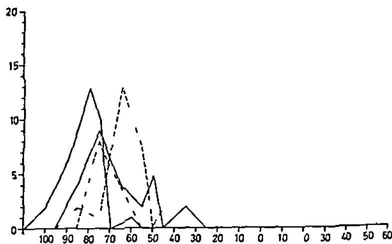


Fig 3

The figure shows the total reflection of ultrasound caused by muscular and fat tissue On the right we have the control curve obtained in water and on the left the echo amplitude curves obtained with muscular tissue (continuous line) and fat tissue (discontinuous line)

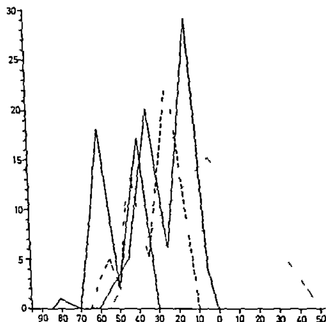


Fig 4

The figure represents the curves that were obtained when the ultrasound passed through muscular tissue (continuous line) and fat tissue (discontinuous line) at an angle of approximately 60 The maxima may considerably surpass the maximum of the control curve on the right.

than in the control curve and in relation to the control curve they seem to have become somewhat dislodged

Comments

The results show that at a particular angle of incidence orbital muscular and fat tissues may cause a total reflection in ultrasound In spite of the fact that we were not able to examine more than one cross section of the sound field with the steel ball relatively high echoes were registered It is possible that if several cross sections had been examined even higher echoes could have been found because the sound beam could also become dislodged at the same time that it was reflected

It is by *no means* new to the authors of this paper that after ultrasound has travelled through some tissue a few millimeters thick one can *still* measure

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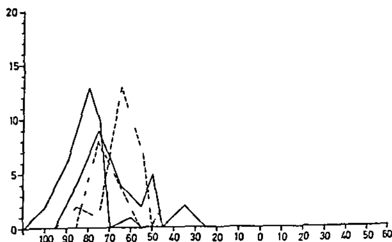


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From the Ophthalmic Department of the University Hospital Turku Finland
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EXPERIMENTAL STUDIES ON THE ECHOGRAM OF THE HUMAN LENS

BY

ARVO OKSALA and ANJA NIIRANEN

The extensive literature on the ultrasonic diagnosis of eye diseases contains only a few works that deal with the acoustic structure of clear and opaque human lenses and the relations between the optic and acoustic structures

According to previous observations an optically clear or almost clear lens is also acoustically homogeneous i e its interior part will not reflect any echoes But if there is a distinct nucleus in a cataract human lens its both surfaces will reflect an echo (*Oksala* & *Lehtinen* 1960) When 3 clear and 26 opaque lenses were examined with a transducer of 18 Mc/5 mm it was discovered that all clear lenses were acoustically homogeneous although the opaque lenses also included 6 acoustically homogeneous specimens (*Oksala* 1961) These results led to the conclusion that the interior part of an opaque lens reflects echoes just in case it contains a clearcut solid nucleus When 15 clear and 15 opaque lenses were examined both clinically and experimentally with a 12 Mc/4 mm transducer all optically transparent lenses were found to be acoustically homogeneous and all cataract lenses acoustically unhomogeneous This led to the fact that on the basis of echograms alone it was possible to determine if the lens would be optically distinctly opaque (*Oksala* & *Varonen* 1965)

Baum (1965) has also verified the acoustic unhomogeneity of the cataract lens and has drawn attention to the diagnostic significance of this phenomenon *Mei* & *Bronson* (1969) examined clinically an unselected series of fifty pre

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sound fields with clear minima and maxima in the far field The appearance of strong maxima may be due to various reflections of ultrasound inside the tissue or to focusing effect of the tissue The changes in the position of the sound fields in relation to the control field may be caused by reflection and refraction that take place inside the tissue

The clinical significance for orbital examinations of the changes in the sound field that have now been discovered cannot be estimated on the basis of this investigation When looked at theoretically refraction reflection and strengthening phenomenon may lead to localization errors in A scan and to a distorted picture in B scan

Summary

At an experimental investigation it was found out that when the angle of incidence is approximately 70° the orbital muscular and fat tissues may cause a total reflection in ultrasound After the ultrasound had passed through muscular or fat tissue one could even in the far field measure echo amplitude curves with high maxima and low minima The maxima may be due to various reflections inside the tissue or to focusing effect of the tissues Total reflection and interference may have clinical significance especially at the ultrasonic examinations of the orbit

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+ 4 C The axial diameter of 43 lenses was measured with a sliding scale The diameter varied between 5 4 and 6 8 mm The axial diameters of the clear lenses were 6 0 6 2 and 6 4 mm

Results

1 The echogram of a clear lens

Fig 1 shows the echogram of the optically clear lens of a 43 year old patient. In all axial examinations the lens proved out to be acoustically homogeneous also when the db reserve = 5 Similarly the optically clear lens of a 50 year-old person was acoustically homogeneous

The third lens came from a 63 year old person whose visus was 1 3 but at a slit lamp examination the center of the lens appeared to be somewhat yellowish Optically the nuclei were a little more clearly outlined than normally Fig 2 shows the echogram of this lens It proves the lens acoustically heterogeneous The change in acoustic impedence at both surfaces of the nucleus is probably so distinct that separate echoes are reflected from them

2 Cataracta ferematura

There were 7 lenses altogether and the respective visus before the operations were 3 × 0 08 and 4 × 0 06 One of the lenses reflected three echoes viz two echoes from the anterior part and one from its posterior surface The echograms of other lenses had 4 5 echoes One of these with 5 echoes is seen in Fig 3 The central parts of the nuclei in these lenses were acoustically homogeneous

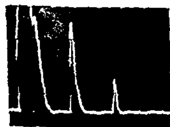


Fig 1

The echogram from the optically clear lens of a 43 year old patient. The initial impulse on the left is followed by the echoes from both surfaces of the lens The lens proper is accoustically homogenous

operative patients with senile cataracts In conclusion of the paper they say that senile cataracts cause abnormal ultrasound patterns the amount of opacity found in the anterior cortex and nucleus by slit lamp correlates semiquantitatively with the ultrasound appearance and the sum of opacities throughout the lens as seen clinically can be predicted by ultrasound with a validity adequate for clinical work

The purpose of the study

On the basis of the earlier results mentioned above we have investigated the echograms of clear and cataract lenses and have made an attempt to clarify the relations between the optic and acoustic structure with reference to various opacities in the lens In addition to that we have studied the attenuation of ultrasound in clear and opaque lenses in comparison with that in water

Research equipment material and method

For our investigation we used Kretztechnik s model 7000 and a 7 5 Mc/2 mm transducer The amplification of the equipment was relatively high i e the db reserve was either 5 or 15

The material comprised 3 clear 7 cataracta feramatura and 36 cataracta matura lenses Clear lenses were obtained from eyes that had been removed because of choroidal melanomas

The transducer was fixed to a stand and beneath it we placed a loop that had been made of copper wire The lenses were then put onto the loop so that the loop itself was outside the sound field The distance of the transducer from the anterior surface of the lens was 5 mm The sound beam was always directed as axially as possible through the lens The examination was carried out in a vessel filled with water One or more photos were taken from an echogram of each lens

The test object that we used to examine the attenuating effect of the lens was a steel ball with a diameter of 1 5 mm This ball was moved so that it passed the center of the transducer at a distance of 25 mm The amplitudes of the highest echoes were compared with one another by the amplification control device of the equipment which is fitted with a db scale In these measurements we used 3 clear and 17 cataracta matura lenses

During the interval between the enucleation and the examination (6 24 hours) the lenses were kept in Ringer solution in a refrigerator at a temperature of

+ 4°C The axial diameter of 43 lenses was measured with a sliding scale The diameter varied between 5 4 and 6 8 mm The axial diameters of the clear lenses were 6 0 6 2 and 6 4 mm

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1 The echogram of a clear lens

Fig 1 shows the echogram of the optically clear lens of a 43 year old patient In all axial examinations the lens proved out to be acoustically homogeneous also when the db reserve = 5 Similarly the optically clear lens of a 50 year old person was acoustically homogeneous

The third lens came from a 63 year old person whose visus was 1 3 but at a slit lamp examination the center of the lens appeared to be somewhat yellowish Optically the nuclei were a little more clearly outlined than normally Fig 2 shows the echogram of this lens It proves the lens acoustically heterogeneous The change in acoustic impedence at both surfaces of the nucleus is probably so distinct that separate echoes are reflected from them

2 Cataracta leramatura

There were 7 lenses altogether and the respective visus before the operations were 3 × 0 08 and 4 × 0 06 One of the lenses reflected three echoes viz two echoes from the anterior part and one from its posterior surface The echograms of other lenses had 4 5 echoes One of these with 5 echoes is seen in Fig 3 The central parts of the nuclei in these lenses were acoustically homogeneous

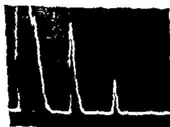


Fig 1

The echogram from the optically clear lens of a 43 year old patient The initial impulse on the left is followed by the echoes from both surfaces of the lens The lens proper is accoustically homogenous

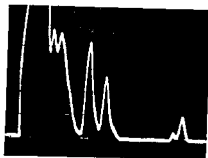


Fig 2

The echogram of the optically almost clear lens of a 63 year old patient with the initial impulse on the left The echoes come from the surfaces of the lens and its nucleus

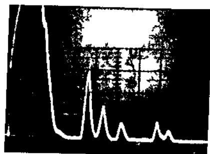


Fig 3

The echogram of a cataracta ferematura lens where the lens reflects 5 echoes The center of the lens is acoustically homogeneous

3 Cataracta matura

Of the 36 lenses one was of the cataracta nigra type All lenses that were examined proved out to be acoustically clearly heterogeneous Among the 70 photos that were taken from the echograms 4 different types could be distinguished These are represented in Fig 4 The echogram in Fig 4 A shows two or three high echo peaks that are reflected from the anterior part of the lens The central part of the lens is acoustically homogeneous and the posterior surface of the lens reflects one or two low echoes In the form that is shown in Fig 4 B and obtained e g from the cataracta nigra case the echogram has clear echoes from both surfaces of the lens and the nucleus while the content of the nucleus seems to be acoustically rather homogeneous In Fig 4 C the lens reflects several compact fairly high and narrow echoes When the position of the transducer was changed the amplitudes and positions of the highest echoes

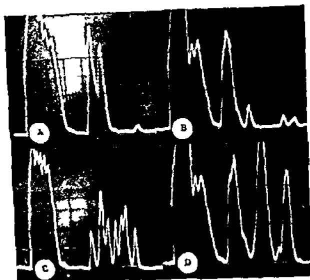


Fig 4

Four different types of echograms that were obtained from cataracta matura lenses In A the anterior part of the lens reflects 2 3 high echoes and its posterior part 1 2 low echoes In B the surfaces of the lens and its nucleus reflect an echo each while the center of the lens is acoustically homogeneous In C the lens reflects several compact echoes and in D there are some less densely situated echoes

showed some variation The lens in Fig 4 D reflects 3 or 4 high and less densely situated echoes

When the attenuation of ultrasound caused by the lens was measured it was discovered that compared with water the amplitude of the highest echo in sound field was attenuated by 12 32 db by the lens In 14 cases out of 19 the decrease in the echo was 21 25 db There was no observable difference in the attenuation of ultrasound between the clear and opaque lenses

Discussion

According to earlier observations an optically clear lens has also been acoustically homogeneous In this investigation however the lens that had been removed from the 63 year old patient with the visus of 1 3 appeared to be acoustically somewhat heterogeneous as both surfaces of the nucleus reflected an echo even if no clear pathological opacity was optically observable Among 7 cata

racta feremature lenses one was acoustically homogeneous apart from the anterior part of the lens

On the basis of clinical ultrasonic investigations we know that the optically clear lens is almost always also acoustically homogeneous As the optic and acoustic examinations and registrations differ a great deal from each other by their very nature it is to be expected that the optic and acoustic examinations of clear or a little opaque lenses at least in older people may yield the kind of controversial results that were obtained from the lens of 63 year old patient The nucleus of the lens may acoustically come out more clearly than at an optic examination and vice versa

All 36 cataracta matura lenses proved out to be both optically and acoustically distinctly heterogeneous On the basis of their form the echograms of opaque lenses could be divided into 4 group In the first two groups the center of the nucleus in the lens was acoustically rather homogeneous as was the case also in cataracta feremature lenses In the third and fourth group the entire lenses were highly heterogeneous

This work shows that on the basis of echograms alone one can often draw rough conclusions of the optic transparency of lenses If a lens is acoustically completely homogeneous it will also be optically clear If the echogram contains only the echoes of the lens and both surfaces of its nucleus the optic transparency of the lens in older people cannot be predicted on the basis of the echograms If the entire area of the lens reflects echoes we have a case of a cataracta matura lens An acoustic examination of the lens may be very useful in cases where an optic examination is impossible due to some opacities of the cornea or a seclusion or occlusion of the pupils

Measurements of the thickness of the lenses indicated that during the storage the lenses had swelled about 2 mm This fact did not affect the echograms of the two optically clear lenses but it is possible that it may have had an effect on the acoustic structure of the clear lens of the 63 year old patient making it a little more heterogeneous It is improbable that this swelling should have changed the decisive factors in the acoustic structure of the cataracta feremature and matura lenses i e the surfaces of the lenses and their nuclei The experimental results obtained from cataracta matura lenses correspond to previous clinical observations

Summary

The material of this study consisted of 46 human lenses out of which 3 were clear 7 cataracta feremature and the rest cataracta matura lenses The optically clear lenses of the 43 and 50 year old persons were also acoustically homo

geneous The 63 year old patient s optically almost clear lens was acoustically somewhat heterogeneous The cataracta ferematura lenses reflected 3 5 echoes but the nuclei were acoustically homogeneous All cataracta matura lenses were acoustically distinctly heterogeneous and their echograms could be divided into four different groups on the basis of their shape There was no observable difference in the attenuation of ultrasound caused by clear or opaque lenses

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THE SYNDROME OF GOLDENHAR AFFECTING TWO SIBLINGS

BY

U KRAUSE

The triad of epibulbar dermoids accessory auricular appendages and pretragal fistulas is termed the Goldenhar syndrome (*Goldenhar* 1952) This triad is often found in combination with other malformations e g hemifacial microsomia coloboma of the upper lids (*Sinha & Mishra* 1950) ptosis (*Proto & Scullica* 1966) coloboma of the iris and choroid (*Ballantyne* 1933) imperforated external auditory meatus (*Stallard & Martin* 1931) and deafness (*Sen Mohan & Gupta* 1969) Numerous vertebral coloumn anomalies are common such as occipitalization of the atlas spina bifida spondylolisthesis etc (see *Gorlin & Pindborg* 1964 *Tost* 1969) The vertebral bony anomalies tend to be overlooked (e g *Leiber & Olbrich* 1966) but are common and *McKusick* (1968) uses the term oculo auriculo vertebral dysplasia synonymously with the Goldenhar syndrome *Sæbo* (1948) describes lipoma conjunctivae in three generations According to *Waardenburg Franceschetti & Klein* (1961) there is nothing to indicate that epibulbar dermoids or lipodermoids might be hereditary in man either alone or combined with the syndrome of Goldenhar *Saraux Grignon & Dhermy* (1963) describe two affected sisters *Proto & Scullica* (1966) three cases of epibulbar dermoids in one and the same family Since few data are available on heredity in the Goldenhar syndrome it seems desirable to report two siblings thus affected

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Case 1 II/3 R L male born 1960 The proband. Auricular appendages were present bilaterally at birth the midwife tied threads round them and they later fell off A dark red elevated tumour was seen likewise at birth on the right side of the nape of the neck The patient therefore entered another hospital in 1963 for the diagnosis Haemangioma nuchae l dx. The tumour was extirpated the pathologist s diagnosis was hemangioma At the age of 7 years impaired vision was found in the left eye and the patient now (*April* 1969) sees an ophthalmologist because the left eye has a peculiar appearance

Right eye Vision 1 4 refraction + 1.5 D Eyelids were normal A small flat lipoma like tumour was seen on the conjunctiva close to the lateral angle. There were no hairs on its surface The cornea was clear the pupil round and responded normally to light. Above, between 11 and 1 o clock there was indistinct thickening of the iris crypts were lacking but the appearance of the iris was elsewhere normal The lens was clear a small remnant of the arteria hyaloidea persistens was seen. The papilla and the eye ground were normal

Left eye Vision 0 9 refraction + 1 0 D Eyelids normal On the conjunctiva temporally below a small non hairy elevation resembling a lipoma appeared near the corneal border In this region the conjunctiva was seen to extend for a distance over the cornea which was elsewhere clear the anterior chamber was of normal depth The pupil was drawn upward to some extent (Fig 1) not completely circular and reacted slowly to light. It was somewhat smaller than the right pupil On retroillumination a defect appeared above in the layer of pigment epithelium the iris stroma extended further out towards the edge of the pupil and showed a partial transition into a greyish membrane Below a normal iris collarette was visible above this collarette approached the pupillary margin with which it seemed to coincide The iris tissue was thickened above and normal crypts were not discernible The vitreous papilla and eye ground were normal

There were distinct remnants of preauricular appendages in front of both ears (Fig 2) and on the left a slight indication of a preauricular fistula No facial asymmetry



Fig 1

Left eye of case 1 The iris is thickened above crypts are absent and temporally above, transition of the iris stroma into a membrane is seen at the papillary margin



Fig 2 A and B
A Right eye of case 1 with remnants of pretragal appendices
B In front of the left ear there is an a remnant indication of a preauricular fistula (arrow)

was observed On the right side of the nape of the neck there was a scar remaining after hemangioma excision X ray films showed a normal thoracic spine.

Case 2 II/1 T L a sister of case 1 born 1956 The patient entered our Clinic in March 1968 for extirpation of a conjunctival tumour at the external angle of her left eye This tumour already present at birth had caused the patient no discomfort It was excised in local anesthesia The pathologist s diagnosis was Lipoma In March 1968 the status was as follows

Right eye Vision 1 4 eyelids and conjunctiva were normal and the cornea clear The iris and the lens as well as the eye ground appeared normal

Left eye Vision 1 4 Eyelids were normal Under the upper lid temporally at the lateral angle there was a lightcoloured slightly prominent tumour A few hairs were seen on the overlying conjunctiva The cornea iris lens and eye ground were normal The ears were normal no preauricular appendages or auricular fistulae were seen The face was physiologically asymmetrical without demonstrable atrophy

The presence of two similar anomalies in two siblings led to the examination of other siblings and the parents (Fig 3)

II/2 J L male born 1957 According to the history this was a case of precipitate delivery and the boy weighing 3500 g at birth had neonatal asphyxia When he was 14 months of age the mother noticed that his right leg was in abnormal position In 1963 he was operated on for spastic hemiplegia (Allongatio tendinei achillei 1 dx)

Vision bilaterally 1 4 The conjunctivae and the iris were normal the lenses clear and the eye grounds showed normal circumstances The ears were of normal appearance and there was no facial asymmetry The right leg was 1 cm shorter than the left

The youngest sibling II 4 J L male born 1964 had an entirely normal ophthal

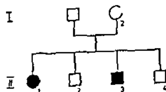


Fig 3
Pedigree of family including two cases of syndroma Goldenhar All these family members were examined. ■ ● affected member → propositus

mological picture The parents (I/1 and I/2) who were not known to be blood relations did not reveal any findings of special ophthalmological interest

Discussion

The syndrome of Goldenhar consists of the complete triad of epibulbar dermoids accessory auricular appendages and pretragal fistulae but the diagnosis is further substantiated if there are coincidental vertebral anomalies The multitude of additional symptoms reported make diagnosis more difficult The presence of incomplete forms of the syndrome has been referred to by *Sugar* (1966) etc

The propositus showed epibulbar dermoids preauricular appendages and unilaterally remnants of preauricular fistulae The diagnosis of the Goldenhar syndrome seems justified in spite of the fact that there was no evidence of vertebral anomalies The iris anomaly in the left eye was of a type not previously described in connection with this syndrome (see *Garner* 1951) It is difficult to decide whether the anomaly was primarily neurodermal or mesodermal The configuration of the iris in the right eye was also pathological and this was evidently a milder form of the same anomaly as affected the left eye

As seen for instance in the case of the proband the syndrome displays varying penetrance for instance the picture differs on the right and the left side Despite the absence of other anomalies it is therefore well warranted to regard the sister s (II/1) dermoid as an atypical form of the Goldenhar syndrome and not as a sporadic case of quite another origin If we accept these conclusions concerning heredity the question as to the localization and properties of the pathological gene arouses interest. We cannot say anything else with certainty than that the gene is not localized in the X chromosome and that it seems to be of recessive type

The spastic hemiplegia of one of the brothers had obviously resulted from a

cerebral lesion This was very likely connected with the precipitate delivery and the postnatal asphyxia Another possibility is that it was a neurological le sion due to vertebral anomaly such a mechanism would be of interest from the point of view of the pathological changes in the vertebral column seen in the syndrome of Goldenhar In such a case however the paresis would present a different clinical picture

Addendum Besides the proband (II/3) another patient attended our Clinic with the Goldenhar syndrome and cutaneous hemangioma The patient was a girl of 2 years showing epibulbar dermoids preauricular appendages facial asymmetry and a mild left sided macrostomy In the temporal region there was a hemangioma 1 × 2 cm in size (Fig 4) A correlation possibly exists between the syndrome of Goldenhar and hemangioma

Summary

Two cases of the Goldenhar syndrome in a brother and sister are reported The brother in addition showed anomalies of the iris of a type not hitherto described in this context and also a hemangioma on the nape of the neck An other brother had spastic hemiplegia probably a result of birth trauma The correctness of the diagnosis is discussed and the site of the pathological gene dealt with The possible correlation between syndroma Goldenhar and cutane ous hemangioma is considered



Fig 4
Two year old girl with syndroma Goldenhar and hemangioma in the left temporal region

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AN APPENDAGE TO THE OPERATING-TABLE FOR OPHTHALMIC MICROSURGERY

BY

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Surgery under an operating microscope is of current interest in ophthalmology In order to be able to utilize the microscope in the best possible way special ar rangement has to be made The standard operating table does not give the sur geon and his assistant a free and convenient access to the operating field Therefore the operating table in use was extended by adding an extra append age This new table leaf consists of a flat piece of wood which fitted into the tracks of the table otherwise used for the X ray magazines A horseshoe shaped support for the wrists of the surgeon and his assistant is attached to the leaf around the place where the patient s head rests The level of the support can easily be regulated and fixed by means of a knob The support can also be removed thereby allowing the table leaf to be pushed under the operating table The leaf and the support are covered by a plastic surface and all metal parts are stainless The leaf is 1350 mm long and 425 mm wide The horseshoe shaped support is 55 mm wide and slightly rounded and the mean radius of its curvature is 165 mm * See fig 1

The new table leaf now in use for more than a year has turned out to be of great help The surgeon and his assistant sit straight across each other in a comfortable position with free space for their knees and easy access to the foot operated control panel

The operating field can be reached freely from both sides and from above

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* This table was manufactured by the workshop of the University hospital Umeå

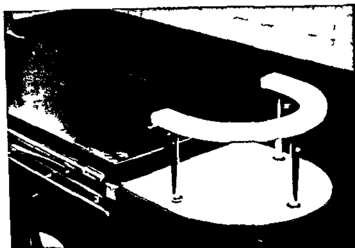


Fig 1
An appendage to the operating table for ophthalmic microsurgery

and the horseshoe shaped support provides a convenient and steady rest for the wrists of the surgeon and his assistant Furthermore the patients complain much less of breathing difficulties than when usual dressing is used

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ULTRASOUND (A-MODE) IN A CASE OF NASAL POSTERIOR SCLERAL ECTASY

BY

HANS FLEDELIUS

Posterior staphylomas or scleral ectasies are usually observed in myopic eyes (2) The diffuse myopic stretching and elongation of the weak posterior pole is much more common than the deep sharpedged staphyloma posticum verum located around the optic disc (12 4)

The depth of the ectasies can be estimated in dioptres by a) direct ophthal moscopy and retinoscopy (13 10) b) refractometry (3) and c) perimetry (the dioptric value of the lens, which when added before the eye makes the refrac tion scotoma disappear) (11 8)

Ultrasound presents another possibility of estimating the lesions as reported in two earlier cases (4 14) With the more elaborate B scan technique the posterior bulbar outline can be reproduced as a soft tissue picture as shown by Trier & Bohm (14) in an excessive myopic patient with bilateral nasal posterior staphylomas and corresponding refraction scotomas The one dimensional A mode ultrasonography makes direct measurement of intraocular distances pos sible This method (in the modification of Gernet (5) with optical determination of the anterior segment of the eye) was used in a case of unilateral peripapil lary scleral ectasy in an non myopic eye reported by François et al (4) (The depth of the ectasy was estimated to more than 20 dioptres or 6 07 mm)

Refraction scotomas were not uncommon in a follow up study of temporal hemianopias published by Riise (9) One of his cases will be reported in more

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detail here The patient presented a unilateral scleral ectasy in the nasal quadrants of an otherwise non myopic eye with normal intraocular pressure Intraocular distances were determined with A mode ultrasonography which was however made difficult by the peripheral location of the ectasy necessitating an oblique direction of the sound beam

Case history

A 48 year old female (J No 3398/69 70) had since early childhood been weak sighted in her left eye but she had not otherwise suffered from ocular disease There was no evidence of squint myopia or astigmati m in her family

Eye examination revealed that eye lids ocular adnexa eye motility pupil reactions intraocular pressure (16 mm in both eyes by applanation) and slit lamp examination were normal and the position of the eyes was normal estimated by the cover uncover test

Right eye

Visual acuity 6,6 + 1 0 sph

Keratometry (Javal Schiotz) ± 0 5 0°

Visual field normal by campimetri and Goldmann perimetry

Ophthalmoscopy normal

Ultrasound examination in the assumed optical axis

anterior chamber	3 33 mm
lens	4 14 mm
vitreous	15 03 mm
axis length	22 50 mm

Left eye

Visual acuity > 6 60 + 2 5 cyl 100

Keratometry (Javal Schiotz) ± 4 0 10

Visual field Campimetry showed a defect in the temporal visual field for small white and coloured objects This was confirmed by Goldmann perimetry (figure 1) wh h demonstrated the temporal defect for small white objects (II,3) only and not for larger targets (white IV 4)

The defect dimini hed when concave lenses were place l before the eye and totally disapp ared w th -8 0 D sph The ectat c fundus thus achieved better optical conditi ns and the refraction nature of the scotoma was established

Ophthalmosc py Figure 2 shows the dioptrical estimation of the left fundus achiev ed with the ophthalmo c pe lenses and confirmed by retinoscopy The normal macular area was focused with about + 1 0 sph. On the nasal side of the t lted and normal ptic d sc with inverse vessel emerge a fundus ectasy was seen with some choroidal atrophy The maximal depth amounted to about – 15 D located 5 disc diameters from

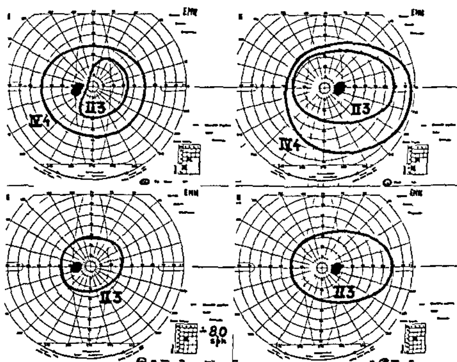
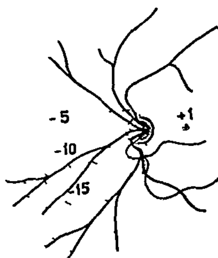


Fig 1

Goldmann perimetry The temporal defect for small white object (II 3) in the left eye (above left) disappears with correction − 8 0 sph (below left) For comparison the isopters of the uncorrected normal right eye (above and below right)



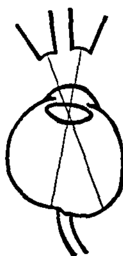


Fig 2 *Fig 3*

Fig 2 Drawing of the left fundus with the dioptrical evaluation achieved with the ophthalmoscope lenses

Fig 3 The two different positions of the transducer (above) and the directions of the sound beam in the left eye

the optic nerve head The ectasy was *diffuse without sharp* demarcation or steep tran sition to the normal fundus

Ultrasound examination from top of cornea to macular area (figure 3)

anterior chamber	3 41 mm
lens	4 06 mm
vitreous	15 6 mm
axis length	23 23 mm

Distance from anterior corneal surface to the bottom of the ectasy in the nasal fun dus (*fig 3) 27 44 mm The ectasy itself thus about* 4 21 mm

Ultrasonographic method

Equipment Kretztechnik Model 7000

The ultrasound measurement procedure grossly followed the outlines of Ok sala (7) and Jansson (6) A *contact glass constructed* at Rigshospitalet by D Ehlers (figure 4) filled with Methocel was interponed between the eye and the ultrasound probe (Ultrasonolux LB 12/PA (1)) making the sound beam traverse a phase homogeneous to sound before entering the eye

The distances between the echoes from the ocular structures were measured primarily in the potentiometer units of the apparatus These units were con verted to metrical values with an interferometer in an initial calibrating procedure 100 units corresponded to a passage of sound through 7 346 mm distilled water by 20 C – or through 7 577 mm anterior chamber and vitreous or 8 116 mm lens substance, and these values were used in this study (The sound velocity in distilled water 20 C is 1486 m/sec in aqueous and vitreous 1532 m/sec and 1641 m/sec in the normal lens (6))

In this special case however the ordinary procedure could not be followed throughout since the sound beam would hit the bottom of the scleral ectasy perpendicularly only by oblique passage through the lens (fig 3) The usual



Fig 4

The *contact* glass (right) and the Ultrasonolux transducer

high lens echoes – indicating the normally desired visual axis direction of the sound – disappeared by the oblique incidence, and the size of the three separate eye parts could not be obtained For the conversion of potentiometer units to metrical values we therefore used a theoretical mean value of ultra sound velocity of 1550 m/sec in ocular tissues, assuming a fair balance between the oblique and thereby longer lens passage and the longer vitreous distance due to the ectasy This mean velocity was calculated from Janssons observa tions on sound velocities in ocular tissues of women aged 40 49 years (6), and it gave the same total axial length of the ectatic eye (23 23 mm) as the previous mentioned isolated values of anterior chamber lens and vitreous

Summary

The actual report is the third one in literature on nasal fundus ectasy examined ultrasonographically The differences from the two earlier published cases (4 14) as regards measurement procedure and anatomical structure have been outlined in the introduction

The dioptric values of the macular area and the nasal fundus ectasy were estimated to about + 1 0 and – 15 D sph by ophthalmoscopy and retinoscopy The corresponding bulbar dimensions were 23 23 mm and 27 44 mm deter mined by A mode ultrasonography The depth of the ectasy itself thus amoun ted to about 4 21 mm

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MEDICAL PRESCRIPTIONS FOR CONTACT LENSES

BY

V DREYER

The demand for contact lenses is so heavy that this must be of concern and in terest to any ophthalmologist The *therapeutic* use of the lenses has been gener ally accepted for many years The *cosmetic* lenses have to a great extent been discredited however it will serve no purpose if the ophthalmologist meets the vain female patient with a sour refusal since there are too many possibilities of obtaining contact lenses without medical supervision In cosmetic cases the ophthalmologist should offer "consumer information" with the primary object of pointing out the present medical contra indications against the use of con tact lenses secondly he should stress the necessity for personal effort on the part of the patient who wishes to become a contact lens wearer and last but not least he must search for a sound motivation this must be present to coun terbalance a fading of the initial enthusiasm The ophthalmologist is ultimately responsible for the welfare of his patient and it will be he who must cure the epithelial damage caused by wrong lenses He must master the technique of fitting since he must be able to point out the errors that have caused a given pathology

Wearing contact lenses is not completely free of risk *Dixon* and his collea gues published in 1966 a study which demonstrated that about one in four thousand of all wearers of contact lenses had lost an eye as a result of compli cations that could with certainty be attributed to the wearing of contact lenses Reversible lesions of the eye amounted to 16 % in this study In 1965 *Reng storff* showed that out of 100 soldiers wearing contact lenses 99 got foreign

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odies under these lenses during their service period Furthermore it was found hat 7 % of these soldiers lost their lenses in the course of time

Principles of Fitting

The percentage of success in treatment with contact lenses varies in the available literature. There is hardly any doubt that the number of successful fittings depends upon the method of designing the lenses In Denmark *Edmund* showed in 1967 that for patients who had their lenses fitted by a skilled optician the succes es were 54 % of all patients who attended the follow up examination In *Gregersen s* study (1967) on weak sighted contact lens wearers the lenses were also used adequately in approximately only half the cases In 1968 *Other* published a report on aphake patients who had a surprisingly high success rate of 73 %

The two decisive factors for a successful prescription for contact lenses are *the cornea s biology* and *its topography* (*Stenstrom* 1968) Evaluating the corneal biology is a medical task as it demands a thorough knowledge of physiology biochemistry and pathology – topics which are all difficult for a technician to comprehend The examination of the corneal topography is concerned with optics as well as with medicine Today the construction of a contact lens with modifications by stages based on a trial and error method and merely consideration of the fluorescein pattern is only necessary with keratoconus patients *and other cases of very irregular corneas It is true* that most current fitting methods include the measurement of the corneal curvature in the visual axis *but this only* The design of the lens is then most often calculated schematically according to an average cornea with a given apical curvature If we act on *average values* we shall be successful in most cases but this method of procedure has its shortcomings when the corneal topography departs from the average furthermore it is not possible to predict which patients are divergent There are many standardized lens designs suited for such schematic fittings there are moulded lenses and turned lenses there are tri spheres and lenses with parabolic variation in the *peripheral curvature there are large and small* thick and thin lenses and there are plastic lenses and gel lenses Every system *has its enthusiastic advocates*

In view of the fact that the topography and biology of the cornea is the most decisive factor in the fitting of contact lenses and that medical research must adopt the fundamental rule of physics – i e to measure all that can be measured and to weigh all that can be weighed – it must be reasonable to make an *effort to map out* the corneal topography of every individual patient Several methods have been put forward whose object is the topographic examination

of corneas The method which in the author s opinion is the quickest and best suited for clinical purposes is the method of *Sampson Soper & Girard* It is based on the use of the topogometer which was developed in 1964 and this method of fitting has been practised in the present study The topogometer consists of a fixation light which can be moved in a co ordinate system with a horizontal and vertical scale on which it is possible to read the size of the area of constant curvature of the cornea – the so called *apical one* The topo gometer is mounted on the Bausch & Lomb s keratometer which also gives the curvature radius of the cornea in any meridian Determinations with the topo gometer have indicated that the apical zone is often situated eccentrically on *the cornea and that the centre of the apical zone – the geometric center* of the cornea (i e half the distance from limbus to limbus) – and the corneal inter section of the visual axis are by no means always common As a contact lens cannot be eccentric itself it is necessary to take into consideration any eccen tricity of the spherical part of the cornea by allowing the lens to rest eccentric ally *Girard* and his co workers maintain that the apical zone must wear the contact lens because it is only possible to form a congruence between the two spherical surfaces in this zone

The question of how a prescribed lens can be tolerated cannot be decided un til a suitable period of adaptation has passed Incomplete information is usually obtained by questioning the patient about his subjective condition only The acceptance of contact lenses varies individually and it is possible to find a satisfied patient with very serious damage to his epithelium During the follow up examination it is necessary to check the visual acuity with the contact lens the clearance of the lens and the state of the naked cornea after vital stain The principal rule is to maintain an intact epithelium by all means and to be vigi lant against corneal edema Only in the case of very irregular corneas – mainly with keratoconus patients – can a certain change of the epithelium be accepted

Before recommending or prescribing the lens it is important to estimate whether in fact it will be of any use to the patient The advantage of contact lenses in the case of unilateral aphakia has been much discussed In this dis cussion it must be stressed that the lenses are conceived as a therapy for ani seikonia and that iseikonia is of no use unless bifoveal binocular vision is pre sent Any medical treatment must always be appraised in relation to the dis advantages and advantages of the treatment in question This is maintained by *Keith Lyle* who in 1953 made an orthoptic study of patients treated for apha kia with contact lenses He believes that an examination of the binocular vision is of great prognostic importance for the success of the treatment An orthoptic examination made in advance may reveal whether suppression or diplopia is present or whether artificial hyperphoria due to decentering of the heavy lens will appear In such cases it is more advisable not to prescribe a contact lens If suppression is present the contact lens will be to no use and in that case it

would be absurd to expose the patient to the inconvenience and risk which is after all associated with contact lenses. *If diplopia is present it must be recognized that being monocular is better than seeing double.*

Results

The data presented here arise in part from patients from The Danish Tribunal of Disablement Insurance and in part from patients referred by eye department and private practice. All the patients who had one contact lens only were *examined with major amblyoscope*. In cases of fusion in a deviating angle only or of small fusional amplitudes the prescription of contact lenses has been rejected to avoid diplopia. This was also the case if suppression was found in the eye that was intended to wear the lens.

Table 1 summarizes all the patients studied. A total of 190 patients have been examined – 58 were primarily rejected for various reasons – 28 did not attend the follow up visit. There remain therefore 89 successful prescriptions *where satisfactory fit and power were found and where the lens could be worn* continuously for 12 hours at least. Only 16 lenses prescribed by opticians could be accepted, a subject to be dealt with below. The first diagnostic group comprises cosmetic lenses and vocational lenses. Here a considerable absenteeism is noticed when *the follow up* examination became due and the reason for this probably was that some patients had abandoned their intention of getting contact lenses as a result of the information as to inconvenience and the risk involved *at the first examination*. The largest group of prescriptions is found in disabling myopia, which is here defined as a myopia exceeding 7 diopters. A number of patients in the group of degenerative myopia were rejected because it was impossible to improve a visual deficiency caused by major central degenerations. *The group of monocular aphakia represents the largest number of* applicants. However, it is also the group where most patients were dissuaded at the outset from wearing contact lenses because of predominant chances of dis*organization of* binocular function. A relatively large number were fitted with contact lenses for bilateral aphakia; in this *group the success has benefited from* the fact that the patients are often old with a corresponding decrease of the corneal sensibility.

Contact lenses are *not the only way of treating* keratoconus. In these respects the degree of this disease can be subgrouped as follows: 1) the mild group where ordinary spectacle glasses are adequate, 2) medium – severe group that has *great advantage* from the use of contact lenses and 3) the most severe group where keratoplasty will be necessary (*Girard & Soper 1965*). *As shown in the* table a fairly large number of patients in the keratoconus group were primarily

Table 1
190 examined patients – grouped according to diagnosis

	Total	Primarily rejected	Absentees	Medical prescript	Approved technician fits
Vocational and cosmetic lenses	32	6	12	14	0
Medical indications High myopia	24	4	2	17	1
Degenerative myopia	21	7	3	10	1
Monolateral aphakia	69	31	6	24	8
Bilateral aphakia	19	3	2	12	2
Keratoconus	11	6	1	4	0
High degree astigmatism	5	0	1	2	2
Keratoplasty	5	1	1	2	1
Neuroparalytic keratitis	2	0	0	2	0
Corneal scars without aphakia	2	0	0	1	1
	190	58	28	88	16

rejected because good vision could be obtained by means of ordinary glasses However continued follow up examinations have been offered these patients and some of them must be expected to change to contact lenses later Other cornea irregularities such as high astigmatism the sequelae of keratoplasty neuroparalytic keratitis with damaged corneal epithelium and finally corneal scars are rare indications but such patients have also proved well suited for contact lenses

Table 2 indicates the most important causes of rejection This shows that in the entire material deficient binocular sight is also the main cause of refusal – comprising about half the number of patients One third was rejected because no improvement of vision could be achieved because of opaque medias or retinal degenerations Finally a minor group was rejected because of contra indicating eye diseases such as an angle closure glaucoma recidivating herpetic keratitis or vigorous blepheratitis which were considered to make the possibility

Table 2

Primary reasons of rejection

Deficient binocular vision	52 %
No improvement of acuity	32 %
Former or foreseen wearing difficulties	16 %

of wearing contact lenses doubtful A very small number were rejected because of difficulties already demonstrated in wearing correct contact lenses this minor group comprises mainly cosmetic cases with weak motivation

Table 3 gives the findings in 94 patients who came to the examination with lenses fitted by technicians In most cases there had been no efficient ophthalmological survey These patients were examined because subjective and objective signs of maladjusted lenses were reported This may explain the fact of only 18 per cent acceptance However the selection shows that a contact lens fitted by a technician exclusively can scarcely *a priori* be trusted to be correct.

On evaluation of the lenses already delivered visual acuity with the lenses the motility and clearance of the lens and epithelial state after vital staining without lens have been evaluated Strangely enough the error most frequently noticed was attributable to the power of the lens nearly half of the lenses presented were of the wrong power The reason may be an imperfect technique of refraction but the most probably reason is that the first refraction made by the technician with the trial lens is done without the use of anaesthaesia of the cornea – thus making the refraction laborious because of an overflow of tears and irritation Damage to the epithelium was observed in one third of the cases and excessive movements in one quarter of the cases

Table 3

Optician's prescription.

Number of patients examined	94 = 100 %
Number of lenses to be modified	[illegible]7 = 82 %
Number of accepted lenses	1[illegible] = 18 %
Reasons for modifications	
Inc rrect power	48 %
Damage t the epithelium	30 %
Lens lag or too large excursions	[illegible] %

Table 4 gives an outline of 116 prescriptions carried out at the clinic on basis of a topogometer examination and refraction with trial lens Approximately half the patients had no previous experience in wearing lenses and the other half were advised on the modification of a prior prescription Only two patients (about 2 %) had to discontinue wearing contact lenses The successful fittings can be made out 76 % but in fact the actual percentage must be well over 80 since it is believed that some of the absent patients were actually successful in wearing contact lenses This opinion was confirmed by a number of calls from the patients or their opticians The "successful prescription criterion does not consider whether the patient later used the lenses after an arbitrary period of observation The criterion of actually being able to wear the lenses during all working hours without damaging the cornea must be the medically important factor and the contact lens should not be blamed if a few patients later give up wearing them for personal reasons

Table 5 shows the distribution of age and sex among the 88 successful prescriptions There are more women than men and an accumulation according to age in the decades of 21 30 years (the myopias) and 51 60 years (the aphakias) Table 6 shows the need for modification of the originally prescribed lens in 88 successful prescriptions 61 % of the patients needed only one prescription and after becoming accustomed they could wear the lens all day In 30 per cent one modification was necessary It was often necessary to alter the over all diameter or the intermediate posterior curve but in rare cases the central posterior curve In 9 % more than two modifications were necessary The need for modifications was equal in novices and in former wearers

Table 7 lists the over all diameters prescribed We find that *Girard s* fitting method results in fairly small lenses and that the predominating diameter is about 9 mm From the table we can also conclude that omitting the measure

Table 4

116 prescribed contact lenses

No prior prescription		63
Re prescription because of imperfect lens from an optician		53
Total		116
Absentees from follow up visits	26	
Discontinued during period of adaptation	2	
		28
No follow up as a percentage of total prescriptions 24 %		
Number of subjects to be reviewed		88

Table 5
88 successful prescriptions

Age	Number	Men	Women
<10 years	2	1	1
10–20 years	13	5	8
21–30 years	26	11	15
31–40 years	12	5	7
41–50 years	11	6	5
51–60 years	16	7	9
61–70 years	6	2	4
>70 years	2	1	1
	88	38	50

Table 6
88 successful prescriptions for contact lenses

	New CL pts	Former CL pts	Total	Per cent
First design satisfactory	28	26	54	61
One modification necessary	15	11	26	30
More modifications necessary	7	1	8	9
	0	38	88	100

Table 7
Prescribed lens diameter

6.0– 7.0 mm	%
8.0– 9.9 mm	80 %
10.0–11.9 mm	13 %

ment of the apical zone and operating instead with a standard lens diameter must in all cases have the consequence that about 20 % of all the prescriptions will not result in correct diameters

Table 8 sums up the prescribed central curvatures Here an accumulation is found in the 42 0 D 43 9 D groups It can similary be concluded that if a posterior curve of about 43 D (or a little below 8 mm) were used as a standard the consequence would be that only a little below half the cases would have turned out successfully

Summary and Conclusion

The data here presented emphasize 1) that it is possible for an ophthalmologist to fit contact lenses satisfactorily as regards wearing period visual acuity and corneal adaptation without too much time consuming effort In more than half the cases the visits have not lasted more than 1½ hours in all

2) that an initial selection of patients suited for contact lenses results in a success percentage that is way above the averages mentioned in literature

3) that an examination of the corneal topography is necessary to obtain a high percentage of success

4) that close cooperation between ophthalmologist and technician is necessary

5) that it must be the ophthalmologist who directs the treatment and that he must know the fitting technique so well that he will be able to discuss necessary modifications if any

6) that future research and improvement of contact lenses is supposed to reach the optimum results if treatment is centralized preferably at hospital centers which employ contact lens opticians

Table 8

Prescribed posterior central curves

40 0–41 0 D	28 %
42 0–43 9 D	47 %
44 0–45 9 D	19 %
46 0–47 9 D	4 %
48 0–49 9 D	0 %
50 0 D	2 %

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INCIDENCE OF CILIORETINAL ARTERIES

BY

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A cilioretinal artery is a terminal artery like the retinal branches from the central retinal artery Presence of a cilioretinal artery involves that dependent on the size of this a larger or smaller region of the retina receives its blood supply *via* the posterior ciliary arteries with no relation to the central retinal artery This may become of practical importance in two situations One is that of total occlusion of the central retinal artery with an at the same time functioning cilioretinal artery and the other that of an isolated occlusion of a fairly large cilioretinal artery

At total occlusion of the central retinal artery a functioning cilioretinal artery can maintain the blood supply to the retinal region involved As this region often includes the macula a normal central vision may be preserved of an eye affected by total occlusion of the central retinal artery This is a clinical picture reported several times in the literature since the end of the 19th century It occurs so frequently and is so well known among clinicians that simple cases are no longer published In a series of 37 patients with occlusion of the central retinal artery (*Lorentzen* 1969) one had a functioning cilioretinal artery A special case of this kind was reported by *Andrzejewska* (1967) seen in a patient with macular degeneration of the right eye and a central artery occlusion of the left In the left eye a functioning cilioretinal artery secured the central vision and supplemented the visual field of the right eye thereby enabling the patient to work and move freely about

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Isolated occlusion of a cilioretinal artery was first described by *Hirsch* in *1896* *Since another* 14 such cases have been reported of which 13 are known from quotations by *Hayreh* (1963) while *Gandolfi* (1946) described one case. An account of a fifteenth case is due to *Ferre, De Oliveira & Alterman* (1967)

Table I gives a survey of the incidences of cilioretinal artery noted previously on the basis of ophthalmoscopy

Material and Results

The total series comprised 172 healthy subjects 68 males and 104 females ranging in age from 10 to 79 They were subjected to out patient examination The majority were examined with a view to refractive anomalies while in some cases the examination constituted part of a general examination. The series included none with ophthalmologic abnormalities nor any with fairly pronounced abnormalities of refraction (refraction between + and − 3 D) Direct ophthalmoscopy was performed using a powerful electric ophthalmoscope The series is identical with one employed previously for studying the incidence of spontaneous venous pulsation in the retina (*Lorent en* 1970)

Only arterioles having the following ophthalmoscopic characteristics were included as *cilioretinal arteries* The arteriole turns up at or just within the disc margin and proceeds towards the middle of the disc It then continues crossing the disc margin outwards in the retina running a more or less straight course like any other retinal arteriole Thus along the first part of its course the arteriole forms a hook which has been compared to the handle of a walking stick

Table II shows the number of examined subjects grouped according to sex and the number of discs left and right respectively with cilioretinal artery

In 45 or 26 per cent of the 172 examined subjects one or two cilioretinal arteries were found In 7 or 4 per cent, of the 172 a cilioretinal arteriole was seen on each disc Of the 344 examined eyes 52 (15 per cent) had cilioretinal arteriole on the optic disc Five (9 6 per cent) of these 52 discs presented two cilioretinal arterioles on the same disc the remaining 47 only one

Table III illustrates the quadrantal location of the cilioretinal arteriole on the disc In table IV the cilioretinal arteries have been grouped according to size Only half of the observed cilioretinal arterioles were large enough to be of practical importance with regard to the blood supply of the retina Nearly all the large cilioretinal arterioles were found to play a functional role 94 per cent supplying the posterior pole and often also the macular region by virtue of their temporal origin on the disc.

Table I

Survey of reported incidences of cilioretinal arteriole and author's own observations

Author	Number of subjects examined	Number of eyes examined	Number of eyes *with* cilioretinal artery	% of eyes with cilioret artery	Number of subjects with cilioretinal artery	% of exam *with* cilioretinal artery	Number examined w bilat cilioret artery	% of examined w bilat cilioret artery	% of subjects w *cilioretional* artery having such bilaterally
Randall 1887	Not stated			about 20 %					
Lang & Barrett 1889		48	8	16 7 %					
Elschnig 1897	170	340		about 7 %					
Jackson 1911	500	1000	191	19 1 %	148	29 6 %	43	8 6 %	29 0 %
Salzmann 1912	Not stated			17 %					
Jensen 1936	100	200	16	8 %					
Bullwinkel 1954	ab 500	ab 1000		16 %					
Mann 1957	Not stated					>25 %			
Collier 1957	1000	2000	250	12 5 %	216	21 6 %	34	3 4 %	15 7 %
Mehra 1965	1448	2896	117	4 0 %	100	6 9 %	17	1 2 %	17 %
Lorentzen 1970	172	344	[illegible]2	15 %	4[illegible]	26 %	7	4 1 %	1[illegible] %

Table II

The table shows number examined, number examined with cilioretinal arterioles and percentage frequency of such, grouped according to sex and laterality. The bracketed figures indicate the numbers of discs with *two cilioretinal arterioles*

	Number examined	Number with cilioretinal artery			Number examined w cilioretinal artery	% of examined with cilioretinal artery
		Right	Left	Bilateral		
Males	68	7 (1)	5		12	18 %
Females	104	16 (1)	10 (2)	7 (1)	33	32 %
Males + Females	172	23 (2)	15 (2)	7 (1)	45	26 %
Eyes	344	23 (2)	15 (2)	14 (1)	52	15 %

Table III

Quadrantal locations of 52 cilioretinal arterioles in 45 subjects. Seven bilateral. Five discs each presented two cilioretinal arterioles (bracketed figures)

Quadrant	Number	%
Upper temporal	21 (2)	40
Lower temporal	28 (3)	54
Upper nasal	2	4
Lower nasal	1	2
All	52 (5)	100

Comments

The incidences of cilioretinal arteries arrived at in the present study, namely 15 per cent of examined eyes and 26 per cent of examined subjects, correspond to the values given in the literature. *Jackson* (1911) found cilioretinal arterioles in 19 per cent of examined eyes and 29.6 per cent of examined individuals, *Bullwinkel* (1954) in 16 per cent of examined eyes and *Collier* (195[illegible]) in 12.5 and 21.6 per cent of examined eyes and examined individuals respectively.

It is worth noting, however, that in no more than about half of the cases are the cilioretinal arterioles of such a size that the retinal region supplied by them

Table IV

Distribution according to size of 57 cilioretinal arterioles in 52 eyes of 45 subjects
Large = extending two disc diameters or more (for temporal arteriole to macula or further) from the optic disc
Medium = extending between one and two disc diameters from the optic disc
Small = extending less than one disc diameter from the optic disc

	Right eye	Left eye	Bilateral	All
Large	9	9	4 + 6	28
Medium	13	4	2 + 1	20
Small	3	4	1 + 1	9
All	25	17	7 + 8	57

has any functional influence on the vision This is probably one of the reasons why an isolated occlusion of a cilioretinal arteriole has comparatively rarely been reported in the literature Such an occlusion of a fairly small cilioretinal arteriole may occur without being noticed Another possible cause of the infrequent publication of reports on isolated occlusion of a cilioretinal arteriole is the fact that occlusions of cilioretinal arterioles as such are rarer phenomena than occlusions of the central retinal artery and its branches

Hayreh (1963) pointed out that we cannot definitely conclude that any arteriole located peripherally on the optic disc is a cilioretinal arteriole It may be an early ramification from the central retinal artery However *Elschnig* as early as 1897 showed histologically in 13 cases that arterioles having the ophthalmoscopic characteristics employed in the present study were direct or indirect branches from Zinn s circle in other words originating from the posterior ciliary artery

Cilioretinal arterioles most often make their exit from the temporal disc margin almost equally often from the upper and the lower quadrant In the series under review the cilioretinal arteriole was located temporally in 94 per cent and nasally in 6 per cent Of *Jackson s* (1911) 191 eyes 188 had the cilioretinal arterioles temporally on the disc *Collier* (1957) found temporal location in 87 per cent and nasal in 13 per cent

In the present series the phenomenon was seen in 23 right eyes (60 per cent of right plus left) and in 15 left eyes (40 per cent of right plus left) *Collier* (1957) found the reverse distribution *Jackson* (1911) observed 53 right and 52 left Thus the two eyes seem not to differ with regard to frequency of cilioretinal arterioles

Five discs each showed two cilioretinal arterioles Among these was one disc of one of the seven subjects with bilateral cilioretinal arterioles *Jackson* (1911) among 191 eyes with cilioretinal arterioles found 12 discs with two such arterioles and two with three

Summary

The incidence of cilioretinal arterioles has been studied in a normal series comprising 1,2 subjects (68 males and 104 females) ranging in age from 10 to ,9 Cilioretinal arterioles were found in 45 of the subjects (26 per cent) and 52 of the eyes (15 per cent) These were unilaterally present in 38 subjects and bilaterally in seven Five of the 52 discs presented two cilioretinal arterioles while the remaining 47 discs had only one each 94 per cent of the cilioretinal arterioles made their exit from the temporal quadrants of the disc Only about half of the cilioretinal arterioles are of a size to make the retinal region they supply play a role with regard to the visual function

Mention is made of the significance of cilioretinal arterioles

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FOCAL DERMAL HYPOPLASIA

Ocular and General Manifestations With a Survey of the Literature

BY

METTE WARBURG

In an institution for the mentally retarded I have seen a case of focal dermal hypoplasia (FDH) a syndrome of which 32 cases have been published previously none so far in the ophthalmological literature

Case History

The patient was a 38 year old severely retarded blind and deaf woman She was the last born of 8 siblings and had no known family history of skin or mental diseases Birth was 9 weeks prematurely and birth weight 2500 g (5½ lbs) She had a congenital skin condition which was interpreted as amniotic adhesions During the first year of life an examination (University Eye Clinic, Copenhagen) showed congenital nystagmus clear corneae microphthalmia symmetrical colobomata of the irides and *ectopia of both lenses A supernumerary* finger was removed from the ulnar side of the right fifth finger at age 17

Until age 9 she was able to walk she then substained a fracture of the femur and has since been confined to bed

Hearing was good until age 15 when recurrent discharge occurred due to

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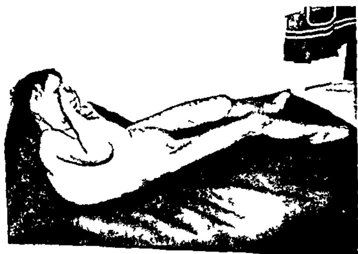
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General condition She was 126 cm (4 feet 1/ inches) high and weighed 19.5 kg (43 lbs) The skull was microcephalic the nose pointed and deviating to the left The teeth were absent the palate flat and the chin well developed Granulomata were present in the external auditory meatus on both sides and a post operative fistula behind the left ear communicated with the middle ear Hearing was presumably absent There was contracture of both sterno cleido mastoid muscles which produced a head tilt towards the left shoulder The neck was short and there was a cervical scoliosis A monstrous dextro convex kypho scoliosis was present in the dorsal region the left curvature was approximately ? centimetres below the iliac crest (Fig 2)

Both breasts were poorly developed and a supernumerary nipple was found on the right breast near the anterior axillary fold No pubic or axillary hair was present The anus was anteriorly displaced the clitoris was absent and the labia majora and minora were very small Scanty menstruation occurred regularly

Skin The skin of entire body was thin dry and scaling It presented numerous small white areas and many brownish patches There were herniations of subcutaneous fat on both calves

Scratch mark was seen everywhere. The hair was scanty and almost absent at the vertex of the scalp but it was not worn off in the nuchal region The lips



Fig

D. sal kyph s s n p tient with f cal dermal hyp plasia. Telangiectasies and patchy p gmentati n can be seen n the back and legs Note ab ence f pubic hair

papillomata in both external auditory meatuses and middle ears Papillomata also occurred when aged 23 on the left labium major and in the coccygeal region They did not recur after curretage The teeth had always been small and deeply set in the gums They were lost at an early age Mentally she was always severely retarded and never learnt to talk She was seen at age 31 and 38 and the findings were identical

Examination (Case rec 1/69)

Eyes There was no perception of light Both eyes were small and deeply set The diameter of the right cornea was 5 mm the left 4 mm Horizontal and vertical nystagmoid movements were present Both corneae showed extensive opacities without vascular invasion In the right eye a more translucent area of approximately 1 mm enabled the observation of a white cataract (Fig 1)



Fig 1

Face of patient with focal dermal hypoplasia syndrome The eyes are microphthalmic the corneae clouded The nose is pointed and deviating the skin of the lips is particularly dry Pigmentations are seen on the breast

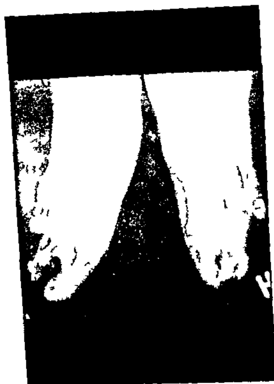


Fig 4
X ray of feet.

Discussion

57 cases of FDH have been reported previously The name was coined by *Goltz et al* (1962) and *Gorlin et al* (1963) found 12 previously reported cases – described under different names Since 1963 ten further cases have been published A survey of these and other cases found in the literature is presented in Table 1 Table 2 is a survey of the principal features of the disease Congenital dysplasia of the skin and extremities are obligate signs of the condition This of course may be a biased point of view as nearly all case histories have been reported by dermatologists. At birth the skin shows scattered lipoma like lesions and atrophic areas which sometimes ulcerate and finally heal by scarring The lesions do not change much during life Focal areas of thin atrophic skin interspersed by telangiectasies or pigmented streaks are seen all over the body and the extremities The lipoma like areas are small reddish yellow or white herniations of subcutaneous fat protuding through defects of the dermis It is common for the affected persons to have papillomata at the mucous membranes

were particularly dry and scaling but papillomata were present only in the ears The patient was capable of sweating

Extremities The patient kept her elbows flexed and her hands in front of her chest but there were no contractures in the arms or legs apart from the hip joints which could not be extended The right hand showed a cutaneous syndactyly between the third and fourth finger The right foot showed syndactyly between the second and third toe and the fifth toe originated 3 centimetres proximally to the other toes The nail was absent on this toe The left foot was a cleft foot with a rudimentary toe on the medial side of the third toe (Figs 3a 3b 4)

Laboratory investigations demonstrated nothing abnormal Paperchromatography of amino acids in urine and serum showed no significant deviations from normal (Professor Lundquist The Biochemical Institute University of Copenhagen) and the karyogram showed a normal karyotype 46/XX (M Mikkelsen M D University Institute of Human Genetics Copenhagen)

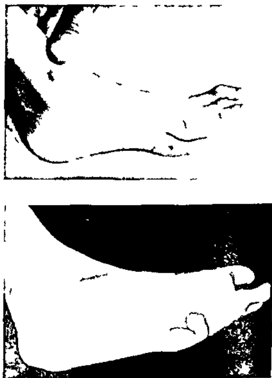


Fig 3

Feet of patient with focal dermal hypoplasia Left foot is split and consists of only three toes There is syndactyly between the second and third toe on the right foot and the third and fourth of the left foot

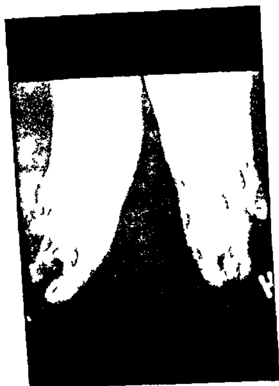


Fig 4
X ray of feet

Discussion

22 cases of FDH have been reported previously The name was coined by *Golt et al* (1962) and *Gorlin et al* (1963) found 12 previously reported cases – described under different names Since 1963 ten further cases have been published A survey of these and other cases found in the literature is presented in Table 1 Table 2 is a survey of the principal features of the disease Congenital dysplasia of the skin and extremities are obligate signs of the condition This of course may be a biased point of view as nearly all case histories have been reported by dermatologists At birth the skin shows scattered lipoma like lesions and atrophic areas which sometimes ulcerate and finally heal by scarring The lesions do not change much during life Focal areas of thin atrophic skin intersperced by telangiectasies or pigmented streaks are seen all over the body and the extremities. The lipoma like areas are small reddish yellow or white herniations of subcutaneous fat protuding through defects of the dermis It is common for the affected persons to have papillomata at the mucous membranes

Table 1
Survey of previously reported cases of focal dermal hypoplasia

Authors	1	2	3	4	5	6	7	8	9
Kruger 1917	M	+			+				
Jessner 1921	F	+			+				
Naegeli 1927	F	+		C	+		R		
Jessner 1928	M	+		S	+				
Marchionini 1932	F	+		P S	+				
Liebermann 1935	F	+	+		+			T	
Cole 1941	F	+	+	S A	—	—	N	T	+
Hurley 1941	F	+	(+)	A				S	+
Wilson 1952, Gold 1958	F	+		S A	+	C	M R	T	
Callagher 1953	F	+		S			M	S T	+
Freeman 1955	F	+		A		C			
Nickel 1956	F	+	+			C	N		
Mannkopf 1957	F	+		S A			M	S	+
Wodnianski 1957	F	+		S A		C M	M	B T	+
Becker 1955	F	+		S		C			+
Rook 1959	F	+							+
Hottinger 1961	F	+	(+)	P	+	C	H R		
Goltz 1962	F	+							+
Gorlin 1963	F	+	+	S C	+	C M O	M R	T	+
	F	+	+	S P	+	C	N		+
Miedzinski 1963	F	+	(+)	S	+				
Solamon 1963	F	+	+	S		C M O	N	(T)	+

	1	2	3	4	5	6	7	8	9
White 1964		+	(+)	S					+
Martin Scott 1965	F	+		S		C	N		+
Holwell 18	F	+		S	—	—	—		—
Braun Fal 1965	F	+	+	S	+	—	(K)	T	+
Bazta 1966	F	+	+	S	+				+
Canala 1968	I	+	+	(A)	+	—	N	T	+
Holden 18	F	+	+	A I S	+	A L M	K	T B S	+
Callen 1967	F	+	+	S	+		N		+
Doug 1968									
Daly 1968	F	+		A S			N	T	+
Walbaum 1970	M	+		A S		—			+
Warburg	F	+		A C I S	+	C I M	M R	B S T	+

Key

Column 1 Sex

Column 2 Typical skin manifestations with focal atrophy pigmentations and telangiectasies

Column 3 Histological evidence of the diagnosis

Column 4 Malformations of the hands or feet A aplasia or hypoplasia of phalanges or metacarpals C cleft foot or cleft hand I polydactyly S syndactyly

Column 5 Papillomata

Column 6 Malformations of the eye A aniridia C coloboma E ectopia of the lens M microphthalmia O optic atrophy

Column 7 Malformations of the central nervous system H hydrocephalus M microcephalus N normal mentality K mental retardation

Column 8 Malformations of the spine and teeth B spina bifida S scoliosis T malformation of the teeth

Column 9 Malformation of the nails

Table 2
Symptoms of reported cases of focal dermal hypoplasia

	Sex	Skin	Phalanges & Metacarpals	Eye	Teeth	CNS	Spine
Sex distribution	29F/3M						
Focal atrophy & pigmentations		33					
Nail dystrophy		21					
Papillomata		17					
Typical histology		15					
Syndactyly			21				
Metacarp /Phal aplasia/hypoplasia			11				
Polydactyly			4				
Cleft hand/Foot			3				
Coloboma				11			
Microphthalmia				5			
Optic atrophy				1			
Ectopia of lens				2			
Abnormal teeth					12		
Microcephaly						6	
Mental retardation						7	
Scoliosis							5
Spina bifida							3

of the mouth the orifice of the external auditory canal the anus and the vagina The nails are thin brittle deformed or wholly or partially absent The teeth are small and often fall out at an early age

The skeletal defects may vary from insignificant shortening of a metacarpus or presence of camptodactyly but are usually severe presenting aplasia or hypoplasia of fingers or toes lobster claw hands or feet syndactyly or polydactyly Scoliosis is not uncommon and microcephalus has been noted

Malformations of the eye have been frequently reported Apart from the trivial sign of squint colobomata have been found in 11 cases and microphthalmia has been noted in 5 cases Optic atrophy aniridia and ectopia of the lens are on record as well

Microscopic examination of the skin from atrophic areas shows a normal epi

dermis and subcutis while there is a nearly total absence of the dermis to the effect that the subcutaneous fat is situated just below the surface of the skin Elastic fibres are degenerated In the papillomatous areas the epidermis is hyperkeratotic and hyperplastic.

Of the 32 cases found in the literature 28 occurred in females

Differential Diagnosis

Holden (1967) probably was right when he said that the FDH syndrome is so striking that there is little confusion with other entities before the syndrome was delimited out as a separate entity is was confused with *Rothmund Thomsen's* disease which also show atrophic skin and telangiectasies In this disease the hands and feet are often small but there are no skeletal malformations It shows a certain affinity to women but 30 % of the cases reported have occurred in males In contrast to the FDH syndrome *Rothmund Thomsen's* disease is not congenital It appears at the age of 3 6 months with an initial erythema The eyes often show cataract and colobomata are not seen

Incontinentia pigmenti (Bloch Sulzberger) also sometimes present focal atrophies of the skin (*Hottinger* 1961) The disease is congenital but the initial lesions are vesicles and bullae which eventually are transformed into pigmented maculae These fade during later years The hair may be scanty and defects of teeth and nails have been reported All affected are females The eyes have not shown microphthalmia or colobomata but may present pseudogliomatous lesions. Skeletal anomalies are not part of this syndrome

Naevus lipomatosus superficialis (Hoffmann Zurhalle) is a congenital skin lesion with hyperplasia of the subcutaneous fat which gives rise to congenital papules under the skin There are no other malformations associated with this syndrome

Progeria is another disease presenting a few months after birth The affected persons are of small stature the skin is atrophic and there is atrophy of subcutis and muscles The hair is thin and alopecia is frequent Teeth and nails are dysplastic The skin lesions are diffuse and not focal there are no skeletal malformations and according to Waardenburg microphthalmia and colobomata are not a part of this syndrome

Cockayne's syndrome sets in during the first few months of life The skin is particularly sensitive to light and traumata and soon presents small localised pigmentations and scars Anhidrosis and dwarfism is common Skeletal malformations do not occur Deafness and blindness due to retinitis pigmentosa are characteristic features and colobomata or microphthalmia do not occur

Congenital stippled epiphyses (*Conradi's* disease) is associated with con

genital patchy erythema in the head and scalp (*Comings et al* 1967) Few affected persons survive but in these the skin shows cicatricial alopecia and follicular atrophoderma The epiphyseal stippling eventually disappears and scoliosis becomes apparent during childhood Cataract has been noted during infancy

Aetiology

It is as yet unknown if FDH is caused by a teratologically active agent or is a genetically determined trait Major chromosomal anomalies can be disregarded as several examinations have shown normal karyotypes It is significant that all but two of the reported 32 cases have occurred in females and *Gorlin et al* (1963) reported a mother of an affected girl to have minor symptoms of the disease Most of the patients published have been children and women with the florid syndrome have not been known to give birth to children Their unfortunate appearance may account for a selective disadvantage further *Gorlin* points out (personal communication) that the reproductive organs of the affected women are often infantile It has been maintained that there is an over representation of abortions in the sibs of the affected patients If a genetical mutation is responsible for the disease it would on the basis of the severe structural anomalies present be supposed to be a dominant one (*McKusick* 1966) and the genetical problems presented by the FDH syndrome would be the same as those of incontinentia pigmenti the oro facial digital syndrome the Wildervanck syndrome and some hereditary cases of congenital cataract with microphthalmia all of which are limited to females

In this syndrome a multitude of theories have been put forward including autosomal dominant heredity with sex limitation (*Gorlin et al* 1963) sex linked dominance with lethality in the males (*Wahrmann et al* 1966 in a case of oro facial digital syndrome occurring in an 47/XXY male) transmission of cytoplasmic inclusions (*Shott & Emery* 1966) or gene duplication as suggested by *Jones et al* (1967) in thyroxine binding globulin of serum

After this paper was completed *Goltz et al* (1970) reported typical cases of focal dermal hypoplasia in two girls one with monolateral coloboma of the iris and choroid

Summary

The 33rd case of focal dermal hypoplasia is reported The patient was a severely retarded blind and deaf woman aged 38 years She presented focal atrophies

pigmentations telangiectasies of the skin and fat herniations The secondary sex characters were poorly developed There was a monstrous dorsal kyphosis lobster claw foot and other malformations of the hands and feet The eyes were microphthalmic with bilateral colobomata of the irides and ectopia of both lenses A survey of previously reported cases and a differential diagnostic discussion is given Aetiological considerations are similar to those presented by incontinentia pigmenti the orofacial digital syndrome the Wildervanck syndrome and certain hereditary cases of congenital cataract and microphthalmia which all are restricted to females

Key words Focal dermal hypoplasia microphthalmia malformations of the eye malformations of the skeleton mental retardation

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COLOURED GLASSES AND COLOUR VISION WITH REFERENCE TO CAR DRIVING

BY

LENNART BERGGREN

In Sweden there is no legal ban whatsoever against car drivers wearing coloured glasses On the other hand it is not permitted for subjects with colour defects of any kind to drive buses (4 7) These facts would clearly be in conflict with each other if there were a conceivable risk that coloured glasses might cause faulty colour reproduction

In the present investigation we have tried to analyze the question of the effect on colour vision by coloured glasses Normal subjects were tested on their *ability to do* an anomaloscopic colour match with different kinds of coloured glasses Their ability to interpret pseudoisochromatic plates was also investigated

It is generally believed and implied that coloured glasses (sun glasses) of good quality reproduce natural colours i e that visible radiation is transmitted as evenly as possible Ultraviolet and infrared rays should be absorbed as much as possible It was surprising and unexpected to find out that coloured glasses even from well known manufacturers were not regularly sold with a transmission spectrum or a relevant description of the characteristics of the glasses in question The glasses were claimed to reproduce natural colours and an information of an average percentage figure of absorption was also given Such a figure suggests an even transmission and is misleading if that is not the case Apparently there seems to be little demand for exact information of transmission properties and the perfection of the glasses is taken for granted

Use of coloured glasses The main purpose of coloured glasses is to prevent

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strong light from reaching the eye The medical use of coloured glasses is li mited chiefly to conditions causing photophobia such as allergic conjunctivitis iritis opacities in the lens and vitreous body and so on

Much of our visual information is based on our capacity to discriminate be tween differences of brightness The differential sensitivity is constant only in luminosities in the middle range and considerable deviations occur in high and low intensities In sunshine the power of discrimination becomes diminished and visual acuity decreases Absorptive glasses used in bright sunshine extends the range of constant differential sensitivity

Another advantage of coloured glasses may be worth mentioning Prolonged stay in strong sunlight decreases the dark adaptation process (5) The intensive bleaching of visual purple over a long period of time results in a utilization of released vitamin A in other parts of the body When twilight sets in the vita min A supply is insufficient and the dark adaptation process will be more sluggish

Coloured glasses are widely used as a protection from glare Glare is caused by the scatter of light from imperfections in the optical media mainly opacities in the lens and the vitreous The stray rays veil the vision and very bright light causes a temporary scotoma The sensation of glare increases with age due to increasing opacities in the optical media (11)

Misuse of coloured glasses Commercial advertising has exploited colour ap pearance concealing effects and other unessential qualities of sunglasses This has unquestionably led to a misuse among certain groups of the population

The conception that the absorption by coloured glasses could do harm to the eye is however not justified Normal illumination changes during the day without glasses are obviously much greater than sunglasses of 15 90 per cent ab orption could ever achieve In other words contrast discrimination can be diminished and in very low illumination also the visual acuity by the use of coloured glasses Permanent harmful effects to the eye however are unknown (10)

Material and Methods

The test subjects comprised ten normal females with an age of 20 50 years

The following different coloured glasses were tested

POL Polaroid 65 per cent absorption grey colour (Polaroid Co U S A)

RBG Ray Ban G 31 69 per cent absorption grey colour (Bausch and Lomb U S A)

RB 3 Ray Ban Shade 3 69 per cent absorption green colour (Bausch and Lomb U S A)

RL 50 Rosa Lux 50 per cent absorption brown colour (Uppsala Optiska Industri Sweden)

RL 70 Rosa Lux 70 per cent absorption brown colour (Uppsala Optiska Industri Sweden)

U 65 Umbral 65 per cent absorption brown colour (Carl Zeiss Germany)

U 85 Umbral 85 per cent absorption brown colour (Carl Zeiss Germany)

UP 65 Umbra Punktal 65 per cent absorption brown colour (Carl Zeiss Germany)

UP 85 Umbra Punktal 85 per cent absorption brown colour (Carl Zeiss Germany)

UG Undefined glasses These glasses were sold in a car service station as sunglasses fit for drivers No quality declaration was given

Transmissive properties in the visible spectral range 400 700 nm of the nine kinds of glasses from the stated manufacturerers are given in fig 1

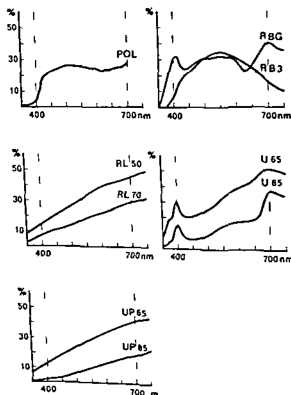


Fig 1
Transmission spectra in the visible region 400 700 nm of *nine different* coloured glasses

Anomaloscopic examination The modern model of the Nagel anomaloscope was used (Schmidt and Haensch Germany) The normal value of the experimental apparatus was 41/16 for the green red/yellow adjustment = a green red quotient of 1 0

Each subject established her own colour match without glasses and with each of the ten test glasses The colour matches were done in a variable order and with five trials for each colour match

The pseudoisochromatic plates by Boström Kugelberg (B K) and Bostrom (II B) are used in the official pseudoisochromatic colour vision test in Sweden There are 20 B K plates and 16 II B plates The subjects were tested without glasses and with the different glasses The method and the subjective and objective evaluation will be further described under Results

Results

The mean results and ranges of the anomaloscope examination expressed in absolute apparatus figures and green red quotients are given in table I and fig 2 It is immediately seen that only Polaroid glasses (POL) and Ray Ban G 31 glasses (RBG) fit a normal Rayleigh equation The mean green red quotient from one of the other glasses was at the protanomalous border and the remaining seven glasses gave "deuteroanomalous green red quotients Glasses with high absorptive properties more markedly affected the colour match

The obvious reasons for these results are the different transmissive properties of the glasses as shown in fig 1 The absorption is not even in the visible part of the spectrum Brown glasses cut off more of the short wave lengths and green glasses cut off short and long wave lengths Only grey glasses show an even absorption It is thus clearly misleading when an average absorption figure is used in order to describe the quality of glasses An example of this is given in fig 3 showing three glasses of similar average absorption but with very different transmission spectra

It should also be pointed out that the general subjective opinion of the test subjects was that the different glasses when used under normal conditions reproduced natural colours The faulty colour reproduction was only revealed by the anomaloscope It has thus been shown that the qualitative as well as quantitative absorption of coloured glasses is of importance in the anomaloscopic colour matches It is also evident that the adjustment variability was greater when glasses with high absorptive properties were used

The ability to interpret pseudoisochromatic plates turned out to be difficult to evaluate in an objective manner If the subjects were allowed enough time they often passed the test also with glasses The test was therefore run without

Table I

Anomaloscopic determinations without and with ten different coloured glasses Ten female subjects Mean apparatus figures and green red quotients are given as well as individual mean ranges and individual adjustment ranges

Type of coloured glasses	Scale readings			Green red quotient	
	Group mean	Range	Individual adjustment Range	Group mean	Range
No glasses	39 8	38 2–47 0	0 – 3 0	1 07	1 15–0 95
POL	39 7	38 2–41 5	0.5– 6 0	1 05	1 15–0 97
RBG	39.5	37 4–42 3	1 0– 6.5	1 08	1 22–0 92
RB 3	47 3	45 7–49.3	1.5– 8 0	0 68	0 62–0 76
RL 50	35 7	33 3–38 7	0.5– 7 0	1.35	1.50–1 15
RL 70	33 8	31 9–35 9	1 0–10 0	1.50	1 65–1.30
U 65	34 6	32 9–36.5	1 0–10.5	1 45	1 55–1 27
U 85	30 9	29 4–33 8	0.5– 8 5	1 74	1 90–1 50
UP 65	35 4	33 7–38 1	1 0– 5.5	1 35	1.50–1 17
UP 85	31 1	8 7–34 3	2 5– 6 0	1 71	1 98–1 42
UG	24 4	22.5–25 6	1.5– 5 0	2.53	2 88–2 40

glasses in the shortest possible time with no errors allowed The test was then repeated with the different glasses noting time and errors See table II During these experiments two things became evident First the experiment had to be done binocularly In monocular speed experiments the test subjects complained of fatigue and blurring and often failed on several plates also without any glasses Secondly the 36 plates became in the long run too familiar to the subjects and a figure could be interpreted without exactly recognizing it A cautious interpretation is that high absorptive coloured glasses seemed to decrease speed and increase the number of errors It was not possible to separate adequately between the different glasses with this method

A subjective judgment of separation between the different glasses in the pseudoisochromatic test is accounted for in table II The subjects were asked to value the test without and with the ten different glasses in figures from 1 to 11 in order of increasing difficulty Thus figure 11 signifies the most difficult test and the figure 1 the easiest test The subjective impression agrees astonishingly well with the degrees of difference of the green red quotients from the normal value established in the anomaloscopic examination The test

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Table II

Judgment of 36 pseudoisochromatic plates without and with *different coloured glasses*
Objective estimation by interpretation time in seconds and *number of wrong answers*
Subjective estimation of test by figures in order of increasing difficulty

	Objective estimation Interpretation time in secs		Number of errors		Subjective estimation (1 11) 1 = easiest test 11 = most difficult test	
	M	Range	M	Range	M	Range
No glasses	61	34–117	0	–	*1 0*	–
POI	74	43–132	1 0	0–2	3 6	2– 9
RBG	67	44–100	1 3	0–3	4 9	3– 8
RB 3	6[illegible]	42–125	1 7	0–4	6 6	[illegible]–10
RL 50	63	32–136	0 6	0–2	4 3	2– 7
RL [illegible]0	62	39–1[illegible]2	1 2	0–3	6 1	4– 8
U 6[illegible]	57	38–108	1 0	0–3	4 7	2– 7
U 8[illegible]	77	50–147	1 7	0–5	8 5	5–11
UP 6[illegible]	63	44–142	1 1	0–5	6 1	2– 9
UP 85	80	49–127	2 4	0–8	9 8	9–11
[illegible]G	[illegible]0	4[illegible]– 91	2 6	0–7	10 7	10–11

subjects did not know the outcome of the anomaloscopic examination when asked to make the subjective judgment

Discussion

The subjective impression that coloured glasses in general are accepted as reproducing natural colours is probably due to the capacity of colour adaptability (10) Colour matches in the anomaloscope reveal the transmissive properties of such glasses and their possible faulty colour reproduction Green red quotients outside the normal range and an increased range of variation in adjustment are similar to the colour matches done by colour defectives of the deuteroanomalous and protanomalous type

In Sweden as well as in several other countries colour defective bus drivers are not permitted To the writer s knowledge there is nowhere any restriction against the use of coloured glasses of any kind of quality for car or bus drivers The inconsistency is obvious from the present results Only permission to

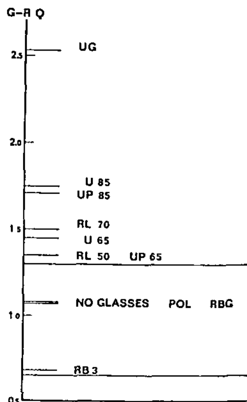


Fig 2
Mean anomaloscopic colour matches by ten female subjects without and with coloured glasses Normal green red quotient = 1 0 Normal range 0 65 1 3

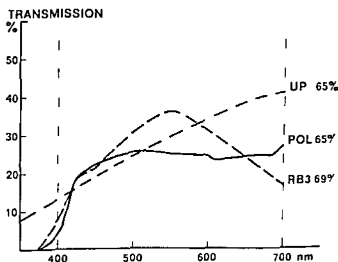


Fig 3
Comparison of transmission spectra of three different glasses with about similar absorption POL 65 % RB 3 69 % and UP 65 65 %

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drive for colour defectives (at least of the anomalous type) or a ban against driving with undefined coloured glasses would make sense

Two circumstances can be pointed out which question the validity of the importance of normal colour vision in traffic A great many drivers undoubtedly wear coloured glasses at least in the summertime However it has not been revealed that the colour of the glasses has played any significant role in violations against traffic laws Nor have controlled large scale studies on colour defective and colour normal drivers been able to show any difference in accident frequency (2, 3 8) In fairness to an opposite opinion it can be noted that although the WHO recommendations in 1956 discounted colour discrimination as a factor in safe driving the question was apparently not settled since there was a sharp division of opinion on the issue in the WHO Symposium 1967 (12) It was concluded by the participants that more information was needed In the latest recommendations in 1969 of the Committee on medical aspects of automotive safety in U S A (1) colour vision is not considered important It is only required that the applicant must distinguish the basic traffic control colours of red green and amber Under artificial conditions (colour vision tests) where colour is the only clue colour defectives make much more mistakes than in actual driving (9)

The controversy in opinions about colour defective car drivers is unnecessary It is the signal system that could and should be made safe for everybody including colour defectives and carriers of coloured glasses It is disappointing that proposals of the use of symbol lights (bars squares diamonds etc) (2 6 9) have not been carried out The use of symbols and hues as remote as possible on the spectrum in street lights flashing signals and rear red lights would lead to much less confusion Such a system would be of great value for safe driving also by colour normal subjects

Summary

Female subjects with normal colour vision 20 50 years of age were tested on their ability to do an anomaloscopic colour match and to interpret pseudoisochromatic plates without and with coloured glasses (sun glasses) of ten different kinds It was found that even glasses of supposed good quality markedly affected colour matching to green red quotients outside the normal range Only with two kinds of glasses the Polaroid glasses and the Ray Ban G 31 glasses was it possible to do a normal colour match The interpretation of pseudoisochromatic plates was impaired by glasses with high absorptive properties The findings are discussed mainly in relation to the question of whether colour discrimination plays any role in safe driving

From the Department of Ophthalmology Kommunehospitalet Denmark
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ROSE BENGAL VITAL STAINING

Staining of Cornea and Conjunctiva by 10 % Rose Bengal Compared with 1 %

BY

M S NORN

The first time rose bengal was used in the eye region seems to have been in 1914 (*Romer Gebb & Löhlein*) The dye was used together with safranine and Victoria yellow to combat pneumococcal infection (quoted by *Marx* 1924)

Kleefeld (1919) was the first to use rose bengal as a vital stain for staining corneal ulcer (quoted by *Marx* 1924)

Marx in 1924 and 1926 subjected rose bengal vital staining to a careful study especially the punctate staining seen on the conjunctiva along the ciliary margin (This line I have found it proper to name Marx line (*Norn* 1966))

Sjogren uses 1 % rose bengal for diagnosing ketatoconjunctivitis sicca The classical M D thesis is from 1933

In normal eyes *Sjogren* occasionally finds staining along the ciliary margin on the caruncle the central portion of the semilunar fold and possibly in a minor proportion on the bulbar conjunctiva nasal to the cornea

In various studies (*Norn* 1962 1964 A 1969 B) I arrived at the result that rose bengal stains degenerate cells The cell nucleus assumes an intenser red colour than the cytoplasm Cells are stained at different intensities slightly degenerate cells assuming a weaker colour than highly degenerate cells Dead cells get an intense red colour

Mucus is likewise stained by rose bengal Double staining with rose bengal and the mucus specific alcian blue gives a specific colouring degenerate cells become red (rose bengal) and mucus blue (alcian blue)

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tensely in all the regions studied cornea, bulbar conjunctiva semilunar fold caruncle inferior fornix inferior tarsus and conjunctiva along the ciliary margin termed Marx line.

The total material is found recorded in table 2 (the percentage number of eyes stained) and in fig 1 (mean colour intensity in region concerned)

Note that the colour intensities differed appreciably e.g from 0 6 to 1 4 from 1 13 to 2 65 and from 2 35 to 3 25 in other words often a rise of one grade by using 10 % instead of 1 % rose bengal

The higher dye concentration also greatly raised the number of corneae stained Thus for instance only 53 per cent of the corneae were stained by 1 % rose bengal against 79 per cent by 10 % rose bengal The inferior fornix was stained in 4 and 16 per cent respectively

The stainability of the cells depends in other words definitely on the dye concentration

Normal Eyes

In general a vital stained region of the conjunctiva or cornea is reckoned as a sign of a pathological process However conjunctival regions are found which usually become stained even in normal eyes The staining is more frequent and more pronounced using 10 % rose bengal compared with 1 % rose bengal

The frequency of staining and the mean colour intensity are recorded in table 3 for the 43 normal eyes after staining with 10 % rose bengal The colour was weaker on the cornea, bulbar conjunctiva inferior tarsus and Marx line than in the pathological cases

The *cornea* is only weakly stained by rose bengal 1 % In the present series 40 per cent were stained generally of the lowest grade The intensity averaged grade 0 60 in the whole normal series (0 79 in the total series)

Staining was found to be most frequent among the elderly subjects A mean grade above 1 was seen in the subjects over 60 years of age

The slight staining of the cornea of normal eyes by 1 % rose bengal had the form of few red dots close to the limbus nasally (8 cases) below and nasally (6 cases) or elsewhere (3 cases)

The 10 % rose bengal concentration gave staining in as many as 77 per cent and a mean colour intensity of grade 1 7 The number of normal eyes stained rose with increasing age. The great majority of the subjects over 40 showed staining (30 out of 32)

The mean colour intensity was likewise higher the older the subjects *Grouping in 10* year age classes gave mean grades of 0 0 2 1.3 1 6 1 8 2 3 and 3 0 for the 10 20 30 40 50 60 and 70 + 80 year age groups respectively

rose bengal was instilled likewise from a needle mounted tube The drop was placed on the bulbar conjunctiva above and lateral to the cornea while the subject was looking down and nasally

Preliminary investigations have shown that the high rose bengal concentration may cause staining at the site of application, where the undiluted dye drop gets in direct contact with the epithelium before blinking and before the tear flow distributes it evenly in conjunctival fluid and precorneal film

I therefore preferred to apply the 10 % dye solution to an area which usually remains unstained

Unlike this solution 1 % rose bengal seems not to cause extra staining at the site of application

Vital staining after instillation of 10 % rose bengal was studied in the slit lamp graduated and the results were entered in a diagram

Material

A total of 100 eyes of 89 subjects were examined 43 eyes were normal and 57 pathological The diagnoses are shown in table 1

Results

Comparison of vital staining with 10 % and 1 % rose bengal respectively gave the result that the higher concentration stained more frequently and more in

Table 1

Clinical diagnoses of 100 eyes subjected to vital staining by 1 % and by 10 % rose bengal

normal eyes	43
erosion foreign body in cornea corrosion	6
dendritic keratitis	6
other keratitis	10
keratoconj sicca	4
contact lens wearer	3
infectious conj	7
chronic simple conj	7
lagophthalmos ectropion	6
others	8

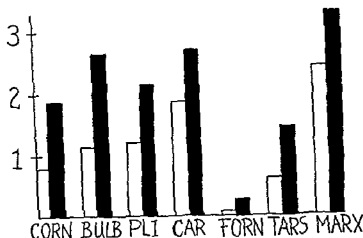


Fig 1

Mean colour intensity on the cornea and *different parts of the conjunctiva* after vital staining by 1 % bengal (white columns) and 10 % rose bengal (black columns) A total of 100 eyes examined Arbitrary grading (ordinate)

Table 3

Mean grades of colour intensity at different sites after vital staining *with 10 % rose* bengal in the normal series (43 eyes) and the total series (100 eyes)

	cornea	bulb conj	fold	caruncle	inf fornix	inf tarsus	Marx line
normal eyes	*1 7*	*2 3*	*2 [illegible]*	*2 6*	*0 4*	*1.3*	*3 0*
total series	1 89	2 65	2 12	2 66	0 26	1 40	3 21

The staining of the cornea in normal eyes by 10 % rose bengal likewise often consisted of rather few red dots *localized close to the limbus nasally (4 cases)* below and nasally (14 cases) or inferiorly (4 cases) In two slight staining was seen elsewhere

In five cases scattered dots were seen all over The remaining four cases were interesting in that the staining after instillation of 10 % rose bengal corresponded exactly to that which may be found in patients with keratoconjunctivitis sicca after instillation of the usually employed 1 % rose bengal (see later)

Table 2

Percentage numbers of eyes stained by the vital stain concerned at the sites concerned

	cornea	bulb conj	fold	caruncle	inf fornix	inf tarsus	Marx line	Number of eyes
rose bengal 1 %	53	64	66	96	4	35	99	100
rose bengal 10 %	79	93	90	99	16	62	100	100
methylene blue	47	70	76	95	33	81	57	100
trypan blue	40	60	70	95	9	48	74	100
bromothymol blue	3	8	8	42	11	23	23	156

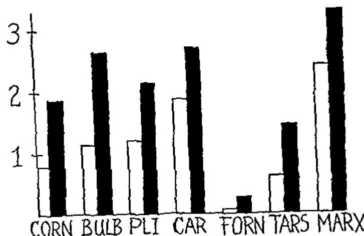


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The *bulbar conjunctiva* is stained more frequently and more intensely th the cornea 1 % rose bengal gave staining in 67 per cent mean grade 1 0 T colour intensity rose perhaps a little with increasing age but apparently not the frequency The sites were most often close to the limbus nasal to the co nea (14 cases) below and nasally (12 cases) or inferiorly (3 cases) Diffuse sicca-like staining was not observed in normals after 1 %

After instillation of 10 % rose bengal staining was more frequent (98 p cent) and more intense (mean grade 2 3) The colour intensity did not ri significantly with increasing age (calculated for 10 year age groups the mea grades were 1 3 1 6 2 7-2 1 2 8 1 9 2 9)

Punctate staining was most frequently seen close to the corneal limbu nasally (6 cases) below and nasally (21 cases) or inferiorly (8 cases)

Using 1 % rose bengal staining was most frequent nasally After instillatio of 10 % the dye most often spread downwards below and nasally thus bein the most frequent site

In thre cases the 10 % rose bengal gave staining temporally close to the sit of application In the remaining four cases sicca like staining was seen

The latter four subjects were all women over 50 with no symptoms

After instillation of the usually employed 1 % rose bengal the cornea re mained unstained, while the bulbar conjunctiva showed few red dots nasa to the limbus corneae

10 % rose bengal on the other hand gave pronounced punctate staining o the exposed part of the cornea extending to the exposed part of the bulbar con junctiva in exactly the same manner as seen after instillation of 1 % rose ben gal into eyes with typical keratoconjunctivitis sicca

It is tempting to regard these normal cases as asymptomatic precursors o keratoconjunctivitis sicca

The *semilunar fold* and the *caruncle* were stained in many cases by 10 % rose bengal (fold 39 out of 43 caruncle all) The colour intensity and fre quency were independent of age and did not differ significantly from the cor responding values in the pathological series

The *inferior conjunctival fornix* was rarely stained (9 out of 43 cases) The staining was independent of age and did not differ from that in the pathologi cal cases

The *inferior tarsus* was stained by 10 % rose bengal in 28 out of 43 cases The colour intensity was not age determined but was less pronounced than in the pathological cases

Marx line was in all cases stained by 1 % rose bengal and more intensely so by the 10 % concentration The colour intensity was perhaps a little lower in the age group under 30 (after 10 % rose bengal the mean grades within 10 year age groups were 1 3 2 0 3 7 3 3 3 5 3 0 3 1) The colour intensity was higher in the pathological cases

Sex Difference

The mean colour intensity was higher in females than in males

The mean grades calculated for all sites were 2 15 for females and 1 71 for males after 10 % rose bengal and 1 11 and 0 91 respectively after 1 % rose bengal

Such a difference was seen even after correction for age variation in the normal series

The sex difference was pronounced for the inferior fornix and the inferior tarsus significant for the caruncle and the semilunar fold and less significant for Marx line while the cornea showed no sex difference

The sex difference seemed to exist within all age classes both after 1 % and after 10 % rose bengal

Pathological Eyes

Corneal Diseases

Corneal defects were stained more intensely by 10 % rose bengal compared with 1 %

In a case of *dendritic keratitis* only few and uncharacteristic elements were visible after instillation of 1 % rose bengal whereas after 10 % several characteristic dendritic elements were seen

One eye affected with chronic *adenovirus keratitis* was stained neither by fluorescein nor by 1 % rose bengal The 10 % rose bengal concentration gave uniformly stained elements scattered over the whole cornea

In a case of punctate superficial keratitis (of *Thygeson s* type) 1 % rose bengal left only few scattered uncharacteristic red elements whereas 10 % rose bengal gave characteristic staining of keratitis elements

One eye with *marginal keratitis* and one with *zoster ophthalmicus* were stained by 10 % rose bengal but not by 1 %

Corrosions of the cornea and conjunctiva were stained more intensely by 10 % rose bengal than by 1 % and the corroded areas were more sharply demarcated from the normal cornea and conjunctiva (Accidents with ammonia, hydrochloric acid nitric acid or slaked lime) In one case corrosion was not recognizable after 1 % rose bengal but the region became intensely stained by 10 % rose bengal

Corneal oedema displayed diffuse punctate staining after instillation of both 1 % and 10 % rose bengal The staining was most intense after the latter

A *corneal graft* remained unstained after both 1 % and 10 % rose bengal Use of the latter is supposed to constitute a more sensitive test for the vitality of the graft than 1 % rose bengal

Contact lens wearers were found to have their cornea bulbar conjunctiva,

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Staining at the Site of Application

The region touched primarily by the 10 % rose bengal drop was exposed to a massive dye concentration until subsequent blinking spread the dye over the entire conjunctival sac and the precorneal film

The intense staining by the 10 % concentration may manifest itself as a local artificial colouring unlike the true vital staining which depends on the de generation of the epithelial cells and which is seen at a greater distance from the site of contact

In eight cases 10 % rose bengal was instilled laterally in the inferior fornix and in four in the outer canthus In seven of the above 12 cases this instillation may have raised the colour intensity recorded in the region concerned

In the remaining 88 cases 10 % rose bengal was instilled above and tempor ally on the bulbar conjunctiva while the subject was looking down and nasally The drop thereby fell on a region which usually is not vital stained

Local staining at the site of application was observed in 65 of the 88 cases often of a weak intensity (grade 1 in 22 grade 2 in 24 grade 3 in 13 grade 4 in 4 and grade 5 in 2 cases) independent of the clinical diagnosis

The stained area was small 1 4 mm in diameter circular or prolonged downwards

In some instances the lower limit was linear horizontal because the concen trated dye drop was stopped in its gravitational flow downwards by the lower ciliary margin.

No similar phenomenon was noticed after instillation of the weaker 1 % rose bengal

Mucus

Rose bengal stains both degenerate cells and mucus Vital staining with 1 % alcian blue after rose bengal shows which of the originally red spots represent mucus and which degenerate cells the former now becoming blue while the latter remain red

After staining first with 1 % rose bengal the normal cornea for instance may show that about half of the originally red dots are mucus and the remain der degenerate epithelial cells (*Norn* 1964 A)

Instillation of 10 % rose bengal gave a more intense colour Subsequent vital staining by alcian blue only disclosed the usually fairly small amount of mucus

The *increased* vital staining by 10 % rose bengal was due to the fact that a greater number of mildly degenerate cells became vital stained while the mucus now constituted a minor proportion only of the vital stained regions

tarsus and Marx line of upper and lower lid more intensely stained by 10 % than by 1 % rose bengal Rose bengal staining shows where the contact lens exerts a pressure being thus useful as an aid to deciding where the lens may need some modification

Keratoconjunctivitis Sicca

In cases with established keratoconjunctivitis sicca even 1 % rose bengal gave characteristic staining in the form of a band across the exposed part of the cornea The band extended further across the exposed part of the bulbar conjunctiva (fig 2)

The colour became more intense with 10 % rose bengal and in some instances extended further also below the cornea

In mild cases of keratoconjunctivitis sicca 1 % rose bengal gave a weaker colour, whereas 10 % rose bengal stained intensely and characteristically

Conjunctival Diseases

The cases of infectious conjunctivitis did not differ significantly from the normal series except that in a small number of cases 10 % rose bengal gave more intense staining inferiorly on the bulbar conjunctiva

Eyes with *chronic simple conjunctivitis* did not differ from the normal eyes

In *ectropion* and *lagophthalmos* better staining of the exposed conjunctiva was obtained with the higher rose bengal concentration Likewise corneal damage was more easily detected with this concentration in *trichiasis* and *entropion*

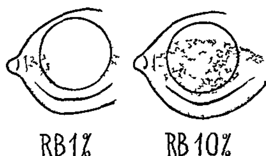


Fig 2

A mild case of keratoconjunctivitis sicca vital stained by 1 % rose bengal (left figure) and the same eye after vital staining by 10 % rose bengal (right figure)

The degrees of solubility of the other vital stains mentioned above are such that use of higher concentrations hardly is permissible.

As a general rule we may say that *10 % rose bengal stains more frequently and more intensely in all the regions than the other vital stains studied*

An exception from this rule is constituted by 1 % methylene blue which stains more frequently and more intensely in the inferior fornix and the inferior tarsus

This more intense staining is however presumably false methylene blue tending to precipitate as granules which are caught by mucus and therefore occur particularly in regions rich in mucus within the inferior fornix and tarsus where the dye drop has been instilled

The main conclusion to be drawn must therefore be that 10 % rose bengal is the best vital stain for detection of degenerate epithelial cells

A scale of *increasing cell degeneration* and cell death can be set up The sound cell is not stained by rose bengal The mildly degenerate cell is stained by 10 % rose bengal only and the more degenerate cell also by 1 % rose bengal while the dead cell is stained by 1 % rose bengal and also by 1 % trypan blue (*Norn* 1969 B)

Rose bengal may disclose degenerate epithelial cells on the cornea and bulbar conjunctiva even in normal eyes This phenomenon increases in frequency and intensity in the higher age classes and is more frequent in the conjunctiva of females than in that of males

The female preponderance of degenerate epithelial cells is possibly due to special properties of the conjunctival fluid and the precorneal film In a previous study I found the precorneal film to be less stable in women than in men (*Norn* 1969 A)

In normal eyes rose bengal stains particularly nasal and lower regions at the limbus corneae

By vital staining with fluorescein micropunctate colouring of the cornea has been shown in 17 per cent of normals (*Norn* 1970) The colouring was seen to rise in intensity with increasing age and to be located in the same region of the cornea.

We may thus conclude that *the region extending nasally below and nasally and inferiorly round the limbus corneae is particularly vulnerable* this region being in normals liable to epithelial cell degeneration of the cornea and conjunctiva and microlesions of the cornea

The phenomenon is not identical with the cold injury phenomenon described by *Kolstad* in skiers The latter is one of rose bengal staining of the lower part of the cornea and bulbar conjunctiva a region bounded above by an upwards convex line Kolstad s phenomenon is perhaps due to freezing of tears accumulated in the middle of the inferior fornix.

The phenomenon described in this paper may possibly be due to physiologi

Side-Effects

In some cases 1 % rose bengal may cause smarting, while in others the instilla tion has no such disagreeable effect It is my impression that rose bengal smarts particularly in the eyes where extensive vital staining is seen e g in kerato conjunctivitis sicca

Rose bengal may precipitate, even in a 1 % aqueous solution These dye grains may cause mechanical irritation

The rose bengal used is from the British Drug House No preservatives nor substances for the sake of isotonia have been added because the dye itself has a certain unknown osmotic effect

In some cases I used 10 % rose bengal without previous local anaesthesia Some of these subjects felt a pronounced smarting pain, while a small number felt no pain

Previous novesin anaesthesia seems to cause no artificial vital staining No more does it alter the wetting properties of the precorneal film (*Norn* 1969 A)

Compared with the usually employed 1 % rose bengal, the 10 % concentra tion naturally has the disadvantage that it may give undesired colouring of eyelids cheek fingers and clothes To avoid this I used the needle mounted tube with its smaller drop size The needle may however tend to become clog ged from one day to the next owing to precipitations of the concentrated dye solution in the lumen

Vital staining even by 10 % rose bengal declines at a fairly fast rate After 20 30 minutes most of the stained regions have grown pale or lost all colour

Permanent colouring (tattooing) has never been observed after rose bengal

Discussion

The present study comprised a direct comparison of staining with 1 % and with 10 % rose bengal in different regions

In a similar manner I have previously compared 1 % rose bengal with 1 % methylene blue with 1 % trypan blue and with 0 2 % bromothylene blue (*Norn* 1967 A B 1968)

1 % rose bengal thus constituted the basis of a comparison with the stated vital stains

The materials investigated were not identical however For instance the pre sent series included a greater number of normal subjects than the others Nevertheless the mean colour intensity with 1 % rose bengal was approxima tely the same in the four series A comparison is therefore judged to be justi fied

The semilunar fold caruncle and conjunctiva along the ciliary margin (Marx line) were seen to become stained in nearly all the normal eyes

Use of 10 % rose bengal is to be recommended in pathological states where 1 % fluorescein and 1 % rose bengal have given no vital staining

In the series under review instillation of 10 % rose bengal disclosed cases of dendritic keratitis punctate keratitis corrosion and keratoconjunctivitis sicca

Familiarity with stainability in normal eyes is required to be able to interpret the colouring observed especially after instillation of 10 % rose bengal

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cal lagophthalmos during sleep (cf *Howitt et al*, who, however, used fluorescein alone and not rose bengal)

The rising frequency and intensity with increasing age may bear relation to the decreasing tear secretion and cornea wetting time (*Norn* 1969 A)

Rose bengal staining is an important *diagnostic aid in keratoconjunctivitis sicca* It may even be claimed to be the most important diagnostic aid in practice because *Schirmer s* classical tear secretion test is unreliable Schirmer s test gives pathological values in far too many normal eyes especially among elderly individuals (*Norn* 1965)

The 10 % rose bengal concentration is better suited to disclose the initial stage of keratoconjunctivitis sicca than the usually employed 1 % rose bengal On the other hand the higher concentration will also disclose asymptomatic cases

10 % rose bengal may thus give occasion to overdiagnosing of the sicca form while on the other hand using 1 % rose bengal one may fail to recognize mild attacks of this disease

The 10 % *rose bengal concentration may disclose pathological* phenomena which are not detectable after instillation of 1 % rose bengal e g mild degrees of dendritic keratitis punctate keratitis corrosion etc

A mixture of 1 % fluorescein and 1 % rose bengal is recommendable for routine staining Fluorescein will then stain epithelial lesions and rose bengal degenerate epithelial cells (*Norn* 1964 C)

If no abnormality is detectable by this mixture supplementary vital staining with 10 % rose bengal may be undertaken The latter vital-stain can disclose mild cases of dendritic keratitis adenovirus keratitis, corrosion keratoconjunctivitis sicca etc

Summary

A total of 100 eyes had first 1 % rose bengal and thereafter 10 % rose bengal instilled

The 10 % concentration stained more frequently and more intensely in all regions than the 1 % Indirectly it was shown that 10 % rose bengal stains degenerate cells more intensely than trypan blue bromothymol blue and methylene blue

In the normal eye degenerate epithelial cells were found peripherally below and nasally on the cornea and the adjacent part of the bulbar conjunctiva (The cornea was stained in 40 and 77 per cent by 1 % and 10 % rose bengal respectively and the bulbar conjunctiva in 67 and 98 per cent)

Prof A Nover Mainz Der Augenhintergrund Untersuchungstechnik und typische Befunde. 2nd enlarged and revised edition Schattauer Stuttgart *1969* *1,6 pages* 148 figures (of this 108 figs in colour) Price DM 42 –

This book is intended as an easily accessible manual giving clear pictures as an aid in assessing ophthalmoscopic findings and it may be emphasized at once that it certainly fulfils its purpose It is unusually well planned written in a lucid style and illustrated by a series of successful photographs of the fundus which demonstrate the various conditions better than a versatile description

In spite of the limited number of pages this book contains a surprising abundance of details and differential diagnostic discussions

It may be earnestly recommended, especially to students and general practitioners and for that matter also to ophthalmologists who want an aid in ophthalmoscopic diagnosis at a reasonable price *Jens Edmund*

Bradley R Straatsma Michael O Hall Raymond A Allen and Frederick Crescitelli The Retina – Morphology Function and Clinical Characteristics UCLA Forum Medical Sciences No 8 University of California Press Los Angeles pp 616

This comprehensive and informative volume contains the proceedings of the conference held November 1966 in connection with the opening of the Jules Stein Eye Institute University of California Los Angeles The amount of knowledge presented by experts is certainly impressive and of the highest standard

Morphology Frank H Moyer Development structure and function of the retinal pigmented epithelium Adolph I Cohen Rods and cones and the problem of visual excitation. Fritiof S Sjostrand The Outer plexiform layer and the neural organization of the retina Raymond A Allen The retinal bipolar cells and their synapses in the inner plexiform layer John E Dowling and Brian B Boycott Retinal Ganglion Cells A correlation of anatomical and physiological approaches Toichiro Kuwabara Blood vessels in the normal retina.

Function Richard W Young The organization of vertebrate photoreceptor cells Michael O Hall and Joram Heller Mucopolysaccharides of the retina Wilfried F H M Mommaerts Circular dichroism and the conformational properties of visual pigments

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Bedrossion E Howard The Surgical and Non surgical Management of Strabismus C C Thomas Springfield Illinois 1969 224 pages 70 figures Price $ 11 50

At present this is one of the most useful books for ophthalmologists and ophthalmolo gists to be who are looking for down to earth and practical knowledge about their squint patients All relevant aspects are presented in a clear concise and easily ac cessible manner Anatomy physiology neurology method of examination non surgical and surgical treatment are given one chapter each Moreover the book contains a chapter relating and defining the nomenclature

The book is extremely didactic and at the same time gives sober assessment of the present possibilities and limitations of strabismus therapy It is stressed for instance that the therapeutic results in accommodative esotropia are better with spectacles than with miotics and that nearly always it is impossible to cure a really fixed abnormal retinal correspondence This is a book which may be earnestly recommended to all who want easily accessible useful sober and sufficient knowledge within the difficult field made up by our numerous squint patients

E Gregersen

Hafferl Anton Lehrbuch der topographischen Anatomie neu bearbeitet von Walter Thiel 3rd edition pp 971 661 illustrations Springer Berlin Heidelberg New York 1969

This topographical anatomy including the international Paris Nomina Anatomica is extremely comprehensive The section on the orbit and orbital region counts 34 pages and appears well suited for students For post graduate teaching of ophthalmologists to be however it is too short As it concerns only topography the ophthalmologist will moreover miss the gross and microscopic anatomy of the eye and eyelids etc

Therefore the book cannot be recommended to ophthalmologists or ophthalmolo gists to be

S Ry Andersen

Milauskas A T Diagnosis and Management of Blowout Fractures of the Orbit Charles C Thomas Springfield Illinois 147 pages price $ 8 50

A diagnosis of blowout fractures – downward displacement of part of the orbital floor unassociated with any damage to the margin of the orbit surrounding the facial bones presupposes a close collaboration between radiologist and ophthalmologist Five out of the 8 chapters of this book are devoted to an accurate description of the radiological technique which may be used with most success paying particular attention to extra conal orbitography and polytomography (hypocycloid tomography) amply illustrated Moreover a brief but sufficient clinical description is rendered with a clear presen tation of the indications for surgery and the surgical technique This book will afford good support in arriving at the correct diagnosis of blowout fracture

Knud Norskov

Prof A Nover Mainz Der Augenhintergrund Untersuchungstechnik und typische Befunde 2nd enlarged and revised edition Schattauer Stuttgart 1969 116 pages 148 figures (of this 108 figs in colour) Price DM 42 –

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Campinchi R Faure P J Bloch Michel E and Haut J L Uveite Phenomenes immunologiques et allergiques Publication de la Societe française d Ophtalmologie. Paris Masson & Cie 1970 Pg 973

This year s report to the French Ophthalmological Society is as usual a very elaborate up to date presentation. The subject is uveitis Of considerable value is the informing compilation of the present experimental data of the immunopathology of uveitis comprising the first 239 pages A special immunological dictionary of 20 pages is found in the end of the volume Clinical manifestations diagnostic procedures ethiology and therapy are dealt with exemplarily and didactily arranged

P Brændstrup

Illustrated Tumor Nomenclature/Nomenclature illustree des Tumeurs/Illustrierte Tumor Nomenklatur 2nd revised edition Prepared by H Hamperl and L V Ackerman (Title contents and preface in English French Russian, German and Spanish legends also in Latin) Springer Verlag Berlin Heidelberg New York With 270 figures XXXV 283 pages 4to 1969 Cloth DM 58 –

The object of this book is to provide illustrations of common neoplasms as they manifest themselves in the various organs and at the same time the most widely accepted term for the tumour concerned It has been endeavoured to avoid overlapping with the programme which is being developed by WHO and which is to result in a uniform histopathological nomenclature for tumours

Some of the illustrations have been borrowed from the various fascicles of the Tumour Atlas of the Armed Forces Institute of Pathology but often appear to be poorer than the originals mainly because of a reduced size On the whole the tumours are illustrated by fairly typical pictures although there are exceptions also in the technical quality of the photographs

All illustrations are black white but since they are to illustrate morphology this is mostly an advantage The choice of nomenclature does not appear to be at all appropriate for instance in the case of the eye where only 2 types are mentioned, viz diktyoma which is certainly not common and retinoblastoma Diktyoma is called medulloepithelioma of ciliary epithelium which is unfortunate as it may occur though rarely outside the ciliary body Retinoblastoma is divided into two types viz with true rosettes and without true rosettes This too is unfortunate as in the same tumour different areas may exhibit from none to numerous rosettes and all transitions The distinction is unnecessary and old fashioned

The book is of no interest to ophthalmologists but may afford some help to the pathologist as a means of rapid reference filling the gap until the WHO series has been completed

O A Jensen

The IV Congress of the European Ophthalmological Society

will be held in Budapest from 17th till 21st April 1972 under the presidency of Mrs. Professor M Radnot The only topics to be discussed are the *functional* examinations in ophthalmology For all information please write to Mrs Professor M. Radnot I Eye Clinic University Medical School VIII Illés u 15 *Budapest, Hungary*

International Council of Ophthalmology and International Federation of Ophthalmological Societies

The *International Council of Ophthalmology* and the International Federation of Ophthalmological Societies met in Mexico at the occasion of the XXI International Congress of Ophthalmology (7 14 March 1970) After having heard a report of Prof Streiff Prof Nordmann, Dr Cuendet and Dr Schellhorn on the information of Ophthalmology they accepted a perforated card for the international coding system of eye disorders

Concerning the contact lenses they accepted the following motion The indication, the prescription, the clinical and optical adaptation and the control of contact lenses must remain medical acts of which only the ophthalmologist has to assume the responsibility Non medical technicians even specialized in optics may only participate in the optical adaptation as paramedical assistants in the doctor s office These assistants have *to be submitted to all the restrictions fixed by the regulations concerning the medical* auxiliaries

They also accepted criteria for the standardization of tonometers

They nominated a committee for review and study of the visual standards for driving as adopted by the Americal Medical Association Committee of medical aspects of automotive safety

Paris has been chosen as the place of the XXII International Congress of Ophthalmology (1974)

The Ophthalmological Societies of Iraq Bolivia Thailand Morocco Lebanon and the Asia *Pacific Academy of Ophthalmology* have been elected members of the International Federation.

Prof Bregeat, Dr Moutinho Prof *Hilton Rocha Prof Sautter Mrs Prof Vannas* Dr Stephen Miller and Dr Hogan have been elected members of the International Council of Ophthalmology

Prof Jules François (Ghent) has been elected president of the International Council of Ophthalmology and of the International Federation of Ophthalmological Societies Dr M Hogan (San Francisco) vice president, Prof Streiff (Lausanne) treasurer and Pr f A Dubois Poulsen (Paris) secretary

XIX SCANDINAVIAN OPTHALMOLOGICAL CONGRESS

Bergen 1969

Address by the president of the Congress, Professor Torstein Bertelsen, M D Bergen, Norway

Ladies and Gentlemen,

It is a great pleasure to welcome so many of my colleagues and their relatives from all the Northern countries, to the 19th *Congress of* Scandinavian Ophthalmologists As probably most of you know, the first meeting was convened *in Stockholm* in June, 1900 Some of the proceedings of this meeting and also parts of the 5th Congress in 1921 took place in Uppsala Apart from this the meetings were held in their entirety in the Capitals until 1954, the year of the 13th Congress The University of Gothenburg had recently been opened and partly to mark this event the Congress was arranged in this town

For the first time in Norway a Congress is now arranged outside the Capital The reason for this decision is the same as in *the case of the* Gothenburg Congress

The idea of a university in Bergen is of a long standing, but it was not until 1946 that it became a reality The main factors forcing the foundation was the accumulation of prospective students during the war years and the increasing demand for academically trained people and in particular for doctors From a very modest beginning when only a few students were admitted each year the University has expanded immensely and now it opens its doors to more than 1000 new students each year About 80 of these are admitted to the Faculty of Medicine and this number will increase in pace with the expansion of the University Hospital

Other new universities have been founded in the Nordic countries, in Umeå Uleåborg and Odense and more will come in the near future Let us hope that some of the future meetings of the Nordic ophthalmologists will be convened in these new university towns I think this might be a very valuable stimulation to the new faculties

By the time of the 1954 Congress the number of participants and lecturers had become so great that it was necessary to divide the meeting into two sections in order to get through the programme This was far from an ideal solution and in 1965 it was decided to have only one section To achieve this meetings should be convened every other year

instead of the previous practise of every third year or even less frequent. The proceedings should be concentrated on a limited number of main topics.

After consultations with the Societies of Ophthalmologists in the Nordic countries it was decided to choose Neuro Ophthalmology and The Orbit as the main subjects for this Congress. These two topics are however so closely interrelated that there has been doubt as to which topic some of the lectures belong.

Neuro ophthalmology is a subject which has developed in pace with the growing importance of neurology in general and neuro surgery in particular. It has become one of the main supporting subjects in these fields. In many places it is already well established as an ophthalmological sub-speciality. The growing number of head injuries mainly due to traffic accidents will certainly increase the importance of this subject, and it will be necessary to establish ophthalmo neurological sections in most large eye departments.

Neither is the orbit of interest only to the eye specialist. Many different pathological processes are capable of spreading to the orbit from adjacent organs, necessitating the close collaboration of specialists in several fields of medicine. In addition to this we have the remarkable hormonal disturbances which presents a problem both to the specialist in internal medicine and to the ophthalmologist.

Our two main subjects show clearly the central position held by ophthalmology in practical medicine, and it is pleasing to see that the problems will be approached from so many different points of view.

A number of lectures on subjects outside the two main topics have also been notified. I consider it important that especially the young ophthalmologists can find in the Scandinavian Congresses a forum where they are allowed to put forward the results of their research, to discuss them with others, to hear opposing points of view, and to be exposed to criticism. I am glad that we not have had to refuse any of these.

Dr Enoksson and Professor Ehlers, two of our colleagues who have been engaged to a very great degree in work on problems related to neuro ophthalmology and the orbit, have agreed to give the introductory lectures on these main topics. I take this opportunity of thanking them for the very considerable amount of work they have done in this connection.

I should also like to express my gratitude to my fellowmembers in the Congress Committee, headed by the secretary general, Dr Henry Aasved, for the interest and enthusiasm they have shown in preparing this meeting.

The Committee has taken the liberty of electing the following chairmen for the individual sessions: Professors Gunnar von Bahr, Poul Brændstrup,

Torstein Bertelsen, Holger Ehlers, Henrik Forsius, Viggo Jensen and Borge Lavætz, Dr Bengt Nyquist Professors Birger Malling Erik Palm, Bengt Rosengren, Henrik Sjogren, Dr Kristjan Sveinsson Professors Thore Thomassen and Jan Ytteborg

Since the last meeting our countries have lost several very capable and highly esteemed colleagues

From Denmark

Holger Hoff and Arne Jessen

From Finland

Lauri Kiianmies and Sigurd Werner

From Sweden

Ulf Wasen

From Norway

Johan Fredrik Harboe and Kristian Gilje

We Honour their Memory

I hereby declare the 19th Congress of Scandinavian Ophthalmologists open

Acta Ophthalmologica Vol 48 1970

THE ORBIT—A SURVEY

By

Holger Ehlers

It is with gratitude but hesitation too I have undertaken the honourable task to open discussion on orbital diseases My scruples are due to the fact that the task in reality is insoluble Concerning each group of diseases in this field is already written books Others are written on exophthalmometry tonography angiography pneumography, pisometry and others again on orbital surgery Problems are so many and so different that nobody can master them all More than a survey in broad outlines cannot be expected

Before I present this survey it is reasonable to recall some peculiar anatomical and physiological features which characterize the orbit and therefore must be of influence on our conception of orbital pathology

The orbit has most space in its anterior part In the top posteriorly the space is very restricted All increase in content has to get its way forward and here the bulb is placed as a valve or a piston which may be displaced Acting to the rear is the pressure of the atmosphere, the eyelids and the pull of the rectimuscles Forward acting is mainly the intraorbital pressure as the pull of the oblique muscles owing to their slanting course only have a slight component forward

The volume of the orbit is 35 cm^3 of this a little more than 7 occupied of the bulb Then 28 cm^3 are left for muscles nerves fat tissue, glands and blood Especially the amount of blood must be remembered as the veins in the orbit are many and form a soft pad for the bulb By his interesting measurements P M Moller found the normal intraorbital pressure 35 mm H_2O and this pressure was rather constant during various conditions if only the bulb was mobile If the bulb was fixed, orbital pressure until 220 H_2O was measured

If P M Moller compressed the content of the orbit by a gradual pressure on a contact lens placed on the bulb the pressure in the orbit stayed rather unchanged *until a compression of 6 mm But* then the

absence of lymph vessels *in the orbit* This may explain some of the characteristic reactions of the orbital tissue especially the ability for edema

The orbit is naturally divided in two parts *the region inside the muscle-cone* and the part outside Pathological processes inside the muscle cone produce an axial proptosis Processes outside the muscle cone produce displacement of the bulb in the frontal plane Space taking processes in the orbit may exert a pressure on the bulb A pressure from the rear may change the refraction several dioptries in hypermetropic direction Pressure against the bulb in the anterior part of the orbit may cause astigmatism of the cornea Ophthalmoscopically the pressure on the bulb *may be seen as fine white lines, sometimes* in concentric formations Such marks may persist for months even if the pressing tumor is removed Pressure on the optic nerve may cause papillary edema, choked disc or athropy followed by *loss of vision*

In the osseuous walls of the orbit there are holes through which nerves and vessels pass in Processes in these passages are accompanied by characteristic symptoms dependent on the anatomy and assembled in syndroms Originally French authors put forward a ' Syndrome de sommet de l orbite Later on more differentiated syndroms are proposed

Canalis opticus loss of vision Ophthalmoscopic and roentgenologic changes

Fissura orbitalis superior 1 trigeminal is affected with neuralgias and disturbances of sensibility in its region The three motoric nerves may be affected although not with equal frequency A grouping of the symptoms in a medial and a lateral has been proposed

Fissura orbitalis inferior 2 trigeminal nerve may be affected Godtfredsen found by tumors in the rhino-pharynx even symptoms from the Eustachian tube or the nasal cavity

Sinus cavernosus is placed so near the apex of the orbit that orbital symptoms are frequent The abducens nerve and the oculomotorius nerve are very exposed, *the ophthalmic nerve too* Vascular symptoms are pronounced (for instance arterior venous communication with pulsating exoftalmos and following subjectively and objectively perceived sounds)

In spite of the real orbital tissue only represents 20 gr and only $^1/_{3}$ $_{00}$ of the weight of the body Its pathology is multitudinous and covers nearly all chapters of the pathology No other tissue elsewhere in the body seems to present so many manifestations from malformations inflammation and circulatory disturbances to haematopoesis endocrinology and lipodystrophy It is peculiar that the morphology and chemistry of the orbital tissue is dependent on hormonal factors Cells fibrils and amor

pressure rose abruptly, presumably because the veins were compressed and the bloodpad empty As the volume of a cone is $\frac{1}{3}\pi r^2h$ the normal amount of blood in the orbit may be approximately 9 or 10 cm³ Bulb and blood together then represent nearly halfpart at the content of the orbit

By attraction of the bulb forward by means of suction on a contact lens P M Møller measured a pronounced reduction at the intra orbital pressure Owing to the conic form of the orbit a protrusion of 1 mm represented a much greater increase in volume than the diminution by 1 mm's enophthalmos The scale of our exophthalmometers should in reality have registered volumes

The orbital fat is a peculiar tissue It is nice lobulated, mobile and easy to displace Its amounts do not directly follow the fat deposits elsewhere It reminds in structure of the subsynoviale tissue around the joints preventing vacuum during movements Under edematous conditions the lobulated orbital fat tissue loses its mobility and the movements of the eye are prevented in a pronounced degree A simple orbital edema may in a purely mechanical way produce severe "pseudo-ophthalmoplegia" The nerves and muscles may be intact In elderly persons the orbital fat owing to the pressure in the orbit may be pressed forward through holes in the orbital septum forming the so called "adipositees orbitopalpebrales" The orbital fat seldom protrudes in the intervals between the recti muscles and become visible as "epibulbar lipoma"

Something fundamental in photography is that the apparatus is quite motionless in the moment of release, the same must hold good of the eye How the pulse wave is prevented from asserting itself in the osseuous limited space is not quite clear, but one or other hindrance there must be In oftalmometry no pulsation of the bulb is visible In tonometry a pulsation is visible when a weight rests on the eye In his first mentioned measurement P M Møller could not register pulse syncrone variations in his curves for the pressure in the orbit In some way the pulse is restrained Probably the damper is to be found in the presence of so many veins, perhaps the peculiar feature of cavernous sinus play a part Krakau and Bynke in their interesting registration of the ocular pulse put a weight of 20 grammes on the eye The ipsilateral pulsations is dependent on the passage in carotis and a slight compression could produce a marked reduction In the prescense of Krakau, Bynke and Horven I have not more to say concerning ocular pulsation

The many veins in the orbit are without valves and their outflow may pass posteriorly (to sinus cavernosus), anteriorly (to vena angularis) or downwards (to plexus pterygoideus) In spite of these abundant possibilities for the outflow, venous stasis can occur A peculiarity is the

Chronic
Granulomatous
Boeck, Hodgkin
Pseudotumor
Parasites (Coccidia) fungus
Special
Tenonitis
Scleritis post

Traumatic

Contusions, Hematoma
Incisions, Stabs
Fractures
Lamina papyracea (emphysema)
Canal optic (atrophy)
Zygomatic (enophthalmos)
Blow out (to sin max)
Luxations
Shotlesions (toys, hunting suicide)
Foreign bodies (traffic, industry)

Vascular

Arterial
Angioma circoid
Aneurysma
Arteritis temporalis
Capillar
Angioma
Venous
Varices
Stasis orbitæ
Aseptic thrombosis
Cavernous angioma
Arterio-venous anastomosis
Pulsating exophthalmos

Systemic diseases

Endocrine
Thyreotoxic hypophysary
Osteopathic
Premature synostosis
Exostosis endostosis

phous substances take part in the changes The cause of orbital alterations may be found far away, as for instance in Horner's syndrome

The principal symptom in orbital diseases is exophthalmos In spite of refined methods, among which Davanger's and Tengroth's exophthalmometry, it is still an intricate thing Normal values are difficult to fix and variations considerable, for instance Knudtzon's and Bertelsen's Often the clinical estimate is decisive Here asymmetry of the skull must not be forgotten, neither unilateral myopia According to Bertelsen, myopia, especially without myopic conus may resemble a proptosis Paralysis of the recti muscles may cause a proptosis too

A few words may be spent on unilateral and bilateral exophthalmos After all they represent two quite different groups of diseases Indeed it shall be admitted, that a bilateral case may start unilateral, but as a principal rule it can be stated that bilateral proptose indicates a systemic disease and a unilateral a local disease

The mysterious condition called 'Pseudotumor of the orbit" has been discussed often Either a tumor has disappeared spontaneously or a supposed tumor could not be found after orbitotomy Presumably different conditions may cause a pseudotumor, for instance insidious inflammations, aseptic thrombosis or a systemic disease

According to the system here set up the orbital diseases are divided in 7 groups Some diseases could properly be placed in other groups as well I hope you will find this survey of use

Malformations

Microphthalmic orbital aplasia
Cyclopia
Cryptophthalmos
Orbito palbral cysts
Dental cysts
Dermoid cysts
Meningo encephalocele
Muscle defects

Inflammations

Acute

Odema		face
Periostitis		nasal sinus
Abscess	from	teeth
Phlegmon		ear
Thrombophlebit		focal

Leucæmic
Plasmacytoma, lymphocytoma
lymphatic infiltrations
Lipodystrofic
Liponecrosis
lipogranuloma
Neurogene
Recklinghausens disease
Horners syndrome

Tumors

Primary
Fibroma, Lipoma, Myoma, Myxoma
Sarcoma, Lipoma
Reticulosarcoma
Tumeur mixte
Secondary
Meningeoma
Glioma, Melanosarcoma
Carcinoma (from lacrymal app)
Glioma, Sarcoma from optic n
From neighbourhood
Lids, nose, rhinopharynx
Metastatic
Carcinoma
Neuroblastoma

Miscellany

Reticoloendothelioma
Eosinophilic osteogranuloma
Letterer Siwe disease
Hand Schuller Christians disease
Juvenil Xanthogranuloma
Granuloma malignum
(Wegeners «midline»)
Cribra orbitalia

Following slides from the collection of the university eye clinic, Copenhagen were demonstrated

Fig 1 Hernia adiposa palpebræ
Fig 2 Atrofia orbitae infantilis
Fig 3 Atrofia orbitae infantilis
Fig 4 Atrofia orbitae infantilis
Fig 5 Cystis orbitae
Fig 6 Cystis orbitae

Fig 1
Albrecht von Graefe (1828–70)

Ueber Complication von Sehnervenentzündung mit Gehirnkrankheiten.

Von

Prof. A. v. G...

Fig 2
The paper in which Albrecht von Graefe presented his hypothesis of choked disc as a sign of intracranial tumour (1860)

From the Department of Ophthalmology, Sodersjukhuset, Stockholm Sweden

NEURO-OPHTHALMOLOGY
A REVIEW

By

Paul Enoksson

Albrecht von Graefe (Fig 1) is the outstanding figure in modern clinical neuro ophthalmology He introduced systematic plotting of visual field defects, gave the correct interpretation of the lesion underlying homonymous hemianopia and was the first to explore the eye ground with the ophthalmoscope invented by *Helmholtz* (1851) *Von Graefe* suggested that a choked disc indicates intracranial tumour (14) and described its transition into optic atrophy in a style which seems unsurpassed in lucidity and accuracy (Fig 2)

The development of clinical neuro ophthalmology has been intimately related to the increasing knowledge of the anatomy of the visual pathway Renaissance artists had a detailed knowledge of muscular anatomy, but when *Leonardo da Vinci* (Fig 3) in his "Quaderni d Anatomia" sketched his concept of the human visual system he was still swayed by medieval misinterpretations He drew a hollow optic nerve connected to three vesicles of the brain, a *cellula phantastica* for perception, a *cellula logistica* for thinking, and a *cellula memorialis* for memory (Fig 4) This was all the more remarkable as *Leonardo* is known to have performed careful dissections of the cerebral ventricles

Now we possess a detailed knowledge of the architecture of the visual system, but we should make it clear to ourselves that this knowledge is in many respects of recent date As late as the turn of the century two schools with prominent members fiercely discussed the problem as to whether an exact topographical representation of the visual fields exists in the occipital lobe The most famous advocate of the hypothesis assuming a diffuse representation in the cortex was *Constantin von Monakow* (Fig 5) in Zurich, known for his demonstration of the lateral geniculate bodies as important parts of the visual pathway To the rival school belonged the German ophthalmologist *Hermann Wilbrand* (Fig 6), who cooperated with the neurologist *A Saenger* in preparing the encyclopedic work 'Die



Fig 5
Constantin von Monakow (1853–1930)

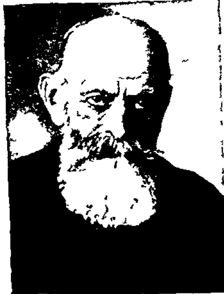


Fig 6
Hermann Wilbrand (1851–1935)

Neurologie des Auges in ten volumes(29) *Wilbrand* once had the opportunity to examine a patient with left sided narrow horizontal homonymous scotomas (Fig 7) When the patient died *Wilbrand* sent the fixated brain to another famous champion of the idea that there is a point for point representation of the visual field in the occipital cortex, the Swedish neurologist *Salomon Henschen* (Fig 8) The latter found a vascular lesion restricted to the floor of the right calcarine fissure(15) He drew the conclusion that here was the representation of the visual field surrounding the horizontal meridian

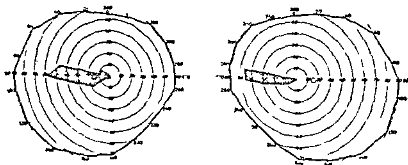


Fig 7
The case of Wilbrand Henschen with horizontal homonymous scotomas caused by vascular lesion of the right calcarine fissure (Wilbrand & Saenger 1917)



Fig 3
Leonardo da Vinci (1452–1519) Self portrait

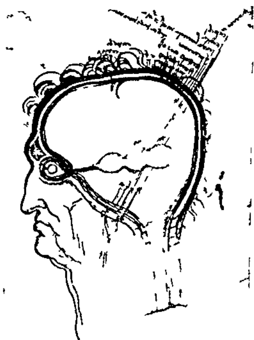


Fig 4
From Leonardo da Vinci's Quaderni d'Anatomia

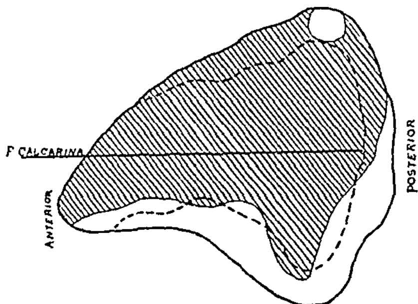


Fig 11
Right area striata in the case of Holmes The portions destroyed by softening are shaded (Holmes 1934) Cf Fig 10

case of bilateral vascular lesions of the calcarine cortex which is of interest when compared with the case of *Wilbrand Henschen*(17) The only parts of the visual fields preserved in this case were wedge shaped remnants along the upper vertical meridian down to and including the fixation area (Fig 10) Postmortal examination showed superficial cortical softening of the striate area except only for the peripheral parts of the lower calcarine lip and the rearmost part of the visual cortex (Fig 11) The horizontal meridian of the visual fields is thus represented at the floor of the calcarine fissure and the vertical meridian peripherally

The pioneer work of *Harvey Cushing* (Fig 12) included almost every field of neurosurgery He played an important part in the practical application of perimetry in topical neurological diagnosis At Johns Hopkins Hospital in Baltimore *Cushing* was once visited by the anatomist *Adolf Meyer* A study of the secondary degeneration following vascular and traumatic lesions of the brain had convinced *Meyer* that the ventral part of the geniculo-calcarine pathway turns forward along the temporal horn before it runs backward towards the visual cortex (Fig 13) If this con ception was right — and it was in accordance with the findings of *Flechsig* in myelogenetic studies — temporal lobe lesions might yield restricted homonymous field defects In *Cushing* s clinic there happened to be a man with a left temporal lobe lesion caused by a bullet which had passed



Fig 8
Salomon Henschen (1847–1930)



Fig 9
Gordon Holmes (1876–1965)

During the first world war the English neurologist *Gordon Holmes* (Fig 9) served as a consulting neurologist to the British Expeditionary Force in France He studied in detail the visual fields in several cases of gunshot wounds of the head and made important contributions to our present conception of the topography in the striate area *Holmes* also described a

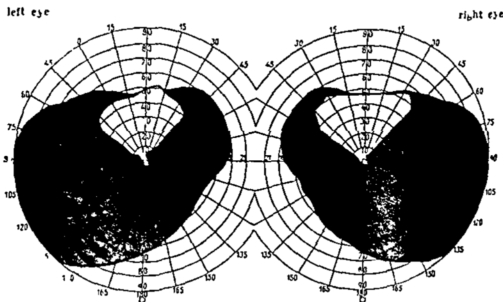


Fig 10
The case of Holmes with wedge shaped remnants of the visual fields along the upper vertical meridians (Holmes 1934) Cf Fig 11

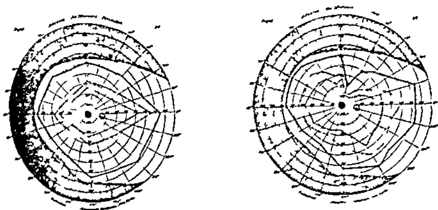


Fig 14
The case of Cushing with traumatic lesion of left temporal lobe Left visual field of right eye on admission of the patient Right visual field re-examined at the suggestion of Adolf Meyer (Cushing 1922)

upper segmental defect to the right of the vertical was recorded (Fig 14) and though in this case the field of the other eye could not be examined, the homonymous upper quadrantanopia this important sign of temporal lobe damage was discovered in principle

In 1912 *Cushing* published his monograph on the pituitary body and its disorders(8) The same year he persuaded a young doctor, *Clifford B Walker*, to join the staff for the purpose of working on ophthalmological problems This proved important for the development of perimetric technique at the clinic(27) Compared with the modern *Goldmann* perimeter *Walker* s instruments may seem primitive (Fig 15) but his investigations left nothing to be desired as far as accuracy and scientific critique are concerned Colour interlacing (Fig 16) had formerly been considered a reliable sign of increased intracranial pressure at *Cushing* s clinic but *Walker* showed that there is no warrant for this concept(26)

However, we do not have to look outside Europe or even Scandinavia to find a brilliant representative of quantitative perimetry at this time *Henning Rønne* (Fig 17) He also performed an important study on the structure of the lateral geniculate nucleus(25)

Supplementary information about the architecture of the visual system has been provided up to the very last years The elegant studies of *Hoyt* & *Luis* are of special interest in two technical respects Like earlier investigators they studied the secondary degeneration of the optic nerves and chiasm following retinal injury This was not, however produced in a crude mechanical way but with the aid of a Zeiss photocoagulator Nor did they study the degeneration by the indirect method of *Marchi* but by the silver impregnation technique of *Nauta* & *Gygax* which makes the de



Fig 12
Harvey Cushing (1869–1939)

through the left eye and had lodged in the petrous portion of the left temporal bone(9) One of *Cushing*'s assistants had examined the right visual field as a matter of routine on the patient's admission to hospital He had not expected any defects and had not found any At *Meyer*'s suggestion perimetry was repeated and additional meridians were now explored An

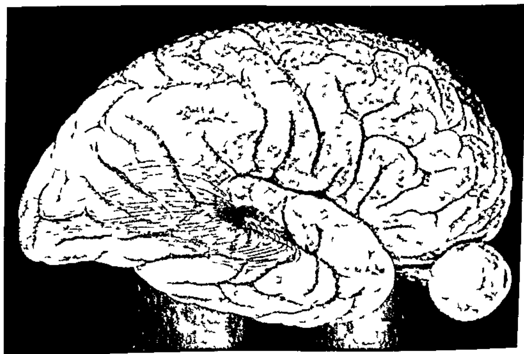


Fig 13
Visual pathway in man drawn by Max Brodel (Cushing 1922)



Fig 17
Henning Rønne (1878–1947)

generating axons themselves visible(19) *Hoyt* found that the arcuate fibres of the retina remain as intact units throughout the optic nerves (Fig 18) and also for a short distance after having entered the chiasm(18) *Hoyt* & *Luis* made beautiful reconstructions of the fibre tracts inside the chiasm, exemplified in Fig 19 which shows how macular fibres are distributed



Fig 18
The course of the arcuate retinal fibres in the left optic nerve chiasm and optic tracts of the monkey (Hoyt 1962)



Fig 15
A perimeter of Clifford Walker's (Walker, 1916)

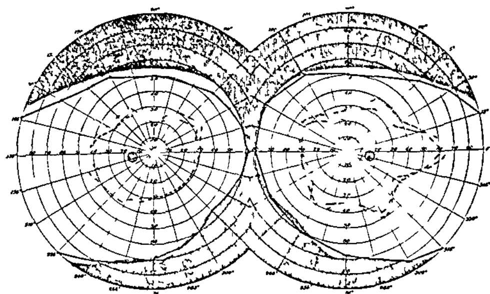


Fig 16
Colour interlacing in the right field once thought to be a sign of increased intra cranial pressure (Walker 1916)



Fig 17
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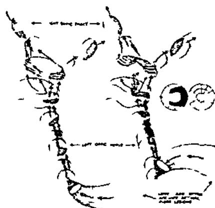


Fig 18
The course of the arcuate retinal fibres in the left optic nerve chiasm and optic tracts of the monkey (Hoyt 1962)



Fig 15
A perimeter of Clifford Walker s (Walker,1916)

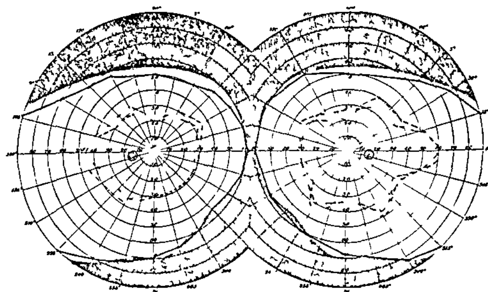


Fig 16
Colour interlacing in the right field once thought to be a sign of increased intra cranial pressure (Walker 1916)

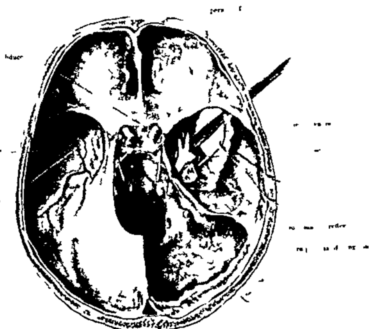


Fig. 21
A neurosurgical approach to the Gasserian ganglion sketch performed by Harvey Cushing (Cushing 1900)

If the ophthalmologist wants to make himself familiar with the clinically important neuro anatomical facts he should not forget to visit the neurosurgical operating theatre Excellent operative sketches can be found in the works of *Cushing, e g* in his monograph Meningiomas written together with the neuro pathologist *Louise Eisenhardt* and published in 1938 a year before *Cushing* s death(10) Fig 21 shows a drawing by *Cushing* demonstrating an approach to the Gasserian ganglion, drawn at a time (1900) when the ganglion was still extirpated in cases of trigeminal neuralgia(7) Apart from the topography of the ganglion it shows other anatomical details of ophthalmological interest The oculomotor nerve can be seen penetrating the dura between the free and attached borders of the tentorium cerebelli a location where it may be compressed in herniation of the brain The abducens nerve can be followed passing freely through the cavernous sinus This course of the nerve explains why abducens palsy is an early sign of malignant nasopharyngeal tumours penetrating the base of the skull a fact which has been amply verified in the monograph of *Godtfredsen*(13) The position of the abducens nerve is still better seen in Fig 22 which is taken from a publication of *D Parkinson*,

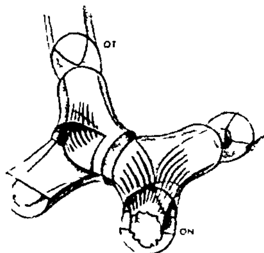


Fig 19
Macular projections through the primate chiasm (Hoyt & Luis 1963)

over the major part of the chiasm The crossing macular fibres do not form small separate bundles at the posterior angle of the chiasm as maintained in many text books

Almost every fact concerning the structure of the visual system known up to 1955 was presented this year in a monumental work by *Stephen Polyak* (Fig 20), born in Jugoslavia, medically educated in Austria and finally working as professor in Chicago He devoted almost thirty years of his life to The Vertebrate Visual System', a beautiful book which is still an indispensable source of knowledge(24) Its 10,000 references suggest the dimension of the work



Fig 20
Stephen Polyak (1889–1955)



Fig 23
Walter Edward Dandy (1886–1946)



Fig 24
Ewald Hering (1834–1918)

eyes, Gesetz der gleichmassigen Innervation beider Augen (16) He founded a famous school for physiologists To this belonged *Alfred Bielschowsky* (Fig 25) who left Europe for America in 1936 He played an important role in his new country, promoting the study of disturbances in



Fig 25
Alfred Bielschowsky (1871–1940)

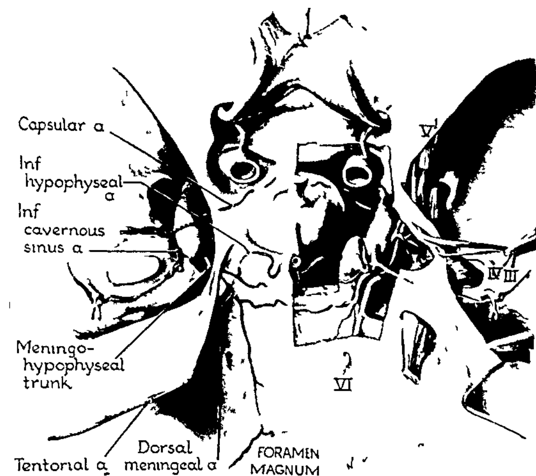


Fig 22
The anatomy of the cavernous sinus (Parkinson, 1965)

the drawing being based on experience of more than 200 cavernous carotid dissections These were performed in order to find a surgical approach to this part of the internal carotid artery(23)

The importance of *Cushing* to the development of clinical neuro ophthalmology has been mentioned already(12) Great contributions were also made by the other neurosurgical genius of America, *Walter Edward Dandy* (Fig 23), who was also responsible for epoch making progress in neuro roentgenology by devising the methods of ventriculography and encephalography In 1921 he described his transcranial surgical approach in the treatment of orbital tumours(11) This was a great step forward as these tumours are often partly intraorbital and partly intracranial

A detailed knowledge of anatomical facts is indispensable for topical diagnosis Physiology, on the other hand, has taught the ophthalmologist to understand many of the symptoms and signs which he will meet in neurological cases *Ewald Hering* (Fig 24), brilliant contemporary of *Helmholtz*, formulated the fundamental law of equal innervation to both

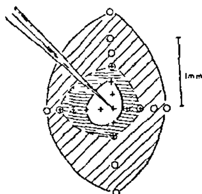


Fig 28
Receptive field of a retinal ganglion cell (Kuffler 1953)

In 1953 *Stephen Kuffler* succeeded in recording potentials from separate ganglion cells in the retina by means of microelectrodes (Fig 28) These were introduced into the eye of the cat in such manner that the eye remained otherwise intact and could be stimulated physiologically(22) This technique was epoch making It was utilized and further developed by *Hubel* & *Wiesel*, who extended their study to the geniculate bodies and the visual cortex(20,21) Their research has revealed fundamental facts concerning the analysing function of the striate area In columns of cells perpendicular to the surface of the brain *Hubel* & *Wiesel* recorded maximal response only with a special field orientation (Figs 29 and 30) They also found cells of different ocular dominance ranging from wholly contralateral to strongly ipsilateral

In 1963 *Carpenter et al* reported the strange observation that discrete lesions of the abducens nucleus in the monkey not only produced abducens palsy but rather a paralysis of the ipsilateral conjugate horizontal gaze (Fig 31) Searching previous literature in this field they found the phenomenon already described in man(6) In 1889 two English neurologists, *Bennett* & *Savill*, had reported a case of paralysis of conjugate ocular movements to the left(1) Autopsy revealed a minute patch of softening in the left abducens nucleus (Fig 32)

Dante Alighieri unexpectedly meets his admired teacher *Brunetto Latino* in the fire rain of Inferno When they part company, *Latino* urgently advises his former pupil

Sieti raccomandato il mio Tesoro

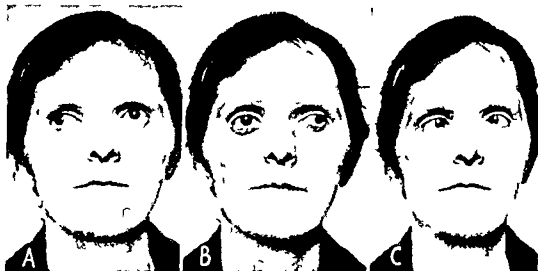


Fig 26
Internuclear ophthalmoplegia (Bielschowsky, 1939)

ocular motility(2,3) In Scandinavia his name is perhaps most intimately connected with the description of internuclear ophthalmoplegia (Fig 26)

1952 is an important year in the history of neuro ophthalmology This year *Åke Bjork* introduced his technique (Fig 27) of electromyographical examination of the human extraocular muscles(4 5)

Fig 27
Electromyographical examination of the internal rectus muscle (Bjork 1955)

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Fig 33
Frank B Walsh

Frank B Walsh (Fig 33) could give the same advice to the ophthalmologists of the world His "Clinical Neuro-Ophthalmology" is a real Tesoro, a treasury, an almost inexhaustible mine of neuro ophthalmological information(28)

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ACTA OPHTHALMOLOGICA VOL 48 1970

From Roentgen Department University Clinic Rikshospitalet
Head Professor dr med T Dale and
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Head Professor dr med *Th Lie Thomassen*

ORBITAL PHLEBOGRAPHY

By

Ivar Paul Enge and *Bjorn Bergaust*

Dejean and *Boudet* introduced orbital phlebography in 1951 (4) Together with *Paleirac* and *Boulieres*(2) they also studied the topographic anatomy and the pathologic conditions of the orbital veins Most recently a number of publications on the subject of orbital phlebography have appeared (1 3 7 8) From a diagnostic point of view it has been stated that the superior ophthalmic vein is the most important orbital vessel This is due to the almost symmetrical appearance of this vein with its extension about 20 millimetres within the muscle cone in close relation to the optic nerve Thus expansive lesions especially those originating from within the muscle cone or from the orbital roof may result in dislocation, distortion or compression of the vein In addition diseases in the veins proper such as varices and occlusions may be directly demonstrated

The patients presenting with unilateral exophthalmos often constitute a difficult diagnostic problem This report describes the use of orbital phlebography in 25 such patients

Technique

A modified percutaneous transfrontal approach(8) was used in 22 patients In 2 cases percutaneous puncture of the angular vein(8) was performed and in 1 further case we applied the internal jugular vein technique (3 5)

The patient is placed in Trendelenburg s position One of the midline forehead veins then usually may be seen or palpated The vein is punctured with a scalp vein needle gauge 19 or 21 to which a polyethylene-tubing filled with normal saline is attached 10 millilitres of Isopaque 350 are injected by hand as rapidly as possible At the same time the patient compresses both anterior facial veins with his index fingers against the maxillary bone Most of the studies were performed on a skull table unit,

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Fig 2
Slight asymmetria Expansion in anterior part of the right orbit? Inconclusive finding



be considered as definitive evidence of pathology since slight asymmetria may occur in normals

Case 2 Haemangioma of the orbit Verified by carotid angiography and operation

Phlebogram (Figure 3) Obvious asymmetria with medial displacement of the right superior ophthalmic vein The angles of the ' vein parallello-



Fig 3
Obvious asymmetria Distortion of the right orbital vein parallelogram due to a haemangioma

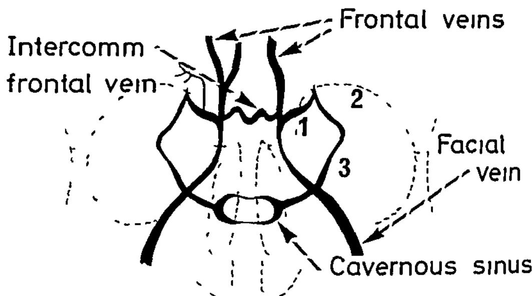


Fig 1
Schematic drawing of normal orbital phlebogram as seen in a 15° submento-occipital view

one exposure made before the start of injection and one at the end of injection of the contrast medium, thus making the subtraction technique possible (3) A 15 degrees submento occipital projection has been the standard view In only a few instances lateral projection was used In a few cases a serial film changer was used

Result and case reports

In 25 patients 27 orbital phlebographies were performed Successful puncture and adequate visualization of the orbital veins were obtained in 20 patients Definitive pathology was revealed in 10 patients, while in 7 cases no abnormality was detected in the orbital phlebogram Inconclusive findings were found in 3 patients Due to difficulties in puncturing the vein, the studies were incomplete in 5 patients

The radiological findings in some of the cases are briefly presented in the following Figure 1 shows a schematic drawing of a normal orbital venogram as seen in a 15 degrees submento occipital view The different segments of the superior ophthalmic vein and its communications anteriorly and posteriorly are demonstrated

Case 1 Slight exophthalmos on the right side No final diagnosis has been reached as yet in this case

Phlebogram (Figure 2) Slight medial and distal displacement of the 1 and 2 segments of the right superior ophthalmic vein This finding cannot



Fig 5
Distortion and partly nonfilling of left orbital vein parallelogram Optic nerve glioma (arrow see text)

shown a vascular expansion, probably haemangioma and small arterio venous shunts

Phlebogram (Figure 6) Angular vein puncture — subtraction picture Complete lack of filling of posterior $^2/_3$ of the left superior ophthalmic vein Some distortion dislocation widening and unsharp demarcation posteriorly of the filled part of the vein, most probably due both to compression from the expansive mass and existing arteriovenous shunts with increased venous pressure

Case 6 Mucocele of the left frontal sinus Verified by operation

Phlebogram (Figure 7) Distal and lateral dislocation of the 1 and 2 segments of the left superior ophthalmic vein caused by the mucocele expanding through the bone defect in the orbital roof

Comments

Orbital phlebography can be carried out utilizing a simple technique and conventional roentgen equipment The examination has no complications and the side effects are reduced to the discomfort accompanying



Fig 4
Nonfilling of the 2 and 3 segment of left superior ophthalmic vein Dislocation and distortion of supra orbital vein branches (arrows) Bone defect in orbital roof Dermoid cyst

gram" decreased, indicating expansive lesion outside the muscle cone (8 9) Case 3 Dermoid cyst of the left orbit Verified by operation

Phlebogram (Figure 4) Only the first segment of the left superior ophthalmic vein is visualized Considerable distortion and dislocation of the supra orbital vein branches (arrows) A bone defect in the orbital roof is seen

Case 4 Optic nerve glioma of the left orbit Verified by operat on

Phlebogram (Figure 5) Non filling of the posterior part (3 segment) of the left superior ophthalmic vein Slight elevation of the 2 segment and increased angle between this and the 3 segment (indicating expansive lesion within the muscle cone), and a "tapering down" appearance on the junction to the nonfilled part (arrow) probably due to compression of the vein from outside

Case 5 Tumour of the left orbit Exophthalmos progressing through a period of 20 years No definitive histological diagnosis has been established as yet in this case Internal carotid angiography left side has

the puncture of the vein and a temporary burning sensation in the orbital regions during and shortly after the injection of the contrast medium The method was originally confined to disease of the orbital veins proper in which the study is elective However, as demonstrated in recent papers from other clinics, we al o have found that orbital phlebography gives valuable information in the evaluation and assessment of expansive lesions of the orbit

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Fig 6

Angular vein puncture Subtraction picture Slowgrowing vascular expansion with small arterio venous shunts on the left side Nonfilling of posterior part of the vein due to the expansion and the A V shunts

Fig 7

Dislocation of the veins due to mucocele originating from the left frontal sinus



Fig 1
Dermoid cyst of right orbit. Diminished size of right orbit and area of diminished desity of bone Sickle shaped desity at margins (arrow)

small vessels (Dilenge and Fischgold 1963) By angiography aneurysms, vascular tumours and malformations are readily shown, and expanding lesions of the orbit may cause vascular displacement The ophthalmic artery has a rather tortuous course however and there are many anatomical variations in the pattern and the distribution of vessels Accordingly tumours in the orbit must be of a considerable size to cause vascular displacement recognizable on the arteriograms Pathological vessels may sometimes be seen in the tumour area Roentgenanatomical investigations have elucidated the normal arteriographic image, and the relation between the ophthalmic artery and the optic nerve (Dilenge *et al* 1965) The following three segments are usually well recognized in the arteriograms

1 Initial segment
2 Optical lateral segment
3 Supra optic segment

(Figures 2a and b)

1 The initial segment consists of an intracranial portion (a) 3–6 mm long an intracanalicular portion (b), marked by a slight narrowing of

ACTA OPHTHALMOLOGICA VOL 48 1970

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RADIOLOGIC EXAMINATION IN ORBITAL TUMOUR

By

Bjorn Bergaust and *Ivar Paul Enge*

Plain X ray films are important in orbital tumours Indicative and sometimes conclusive results may be obtained with manifestations in the bone (Hartmann and Gilles 1959) Diagnosis of type of tumour is possible in some groups of tumours Glioma of the optic nerve, meningeoma of the sphenoidal ridge, osteoma, tumour of the paranasal sinuses and dermoid cysts According to Pfeiffer and Nicholl (1948), dermoids may be distinguished from other causes of proptosis by the characteristical roentgenographic appearance The lesion of the bone is that of an area of diminished density with smooth, regular margins of increased density of bone at the margin

Case 1 A 70 years old man with unilateral proptosis of more than 20 years duration presents a typical case of a dermoid cyst of the orbit (Figure 1) The dermoids probably develop from intradiploic germs, push the periost, and the elevation from the bone may cause the bone formation which is shown on the film as a sickle shaped density

The application of contrast media in the radiological examination of orbital tumour augments the positive results, and new information as to the site, size and nature of the lesion, is added The present contrast methods in orbital X ray are the phlebography, the ophthalmic arteriography and the orbitographies Orbital phlebography is elective for the study of venous disease of the orbit, and also gives valuable information in the study of expansive lesion of the orbit We have made this subject of a special paper (Enge and Bergaust 1970)

Filling of the ophthalmic artery occurs during carotid angiography in up to 98 per cent (Krayenbuhl 1962) The selective injection of contrast media into the internal carotid artery and rapid serial angiography are important for the visualization of the ophthalmic artery The interpretation is facilitated by subtraction technique, improving the contrast of

Case 2 Aneurysm is clearly demonstrated in a case of a typical extradural aneurysm of the carotid siphong (Figure 3a) showing unilateral exophthalmos, papilledema, diminished vision and osseous destruction of the lesser and greater sphenoidal wings (Figure 3b)

Displacement of the arteries is demonstrated by the following two cases

Case 3 Glioma of the optic nerve of a 55 years old man caused an upward concave arch of the opticolateral segment and the intra-orbital portion of the initial segment and also a slight irregularity of the lumen (Figure 4)

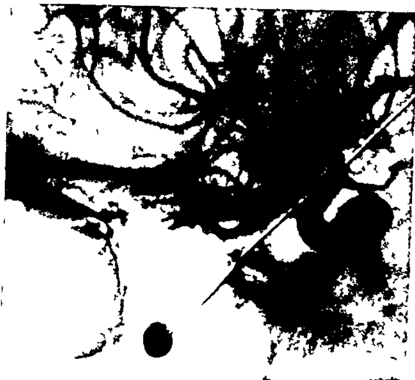
Case 4 A great dermoid cyst of the orbit in a 40 years old man nearly filled the upper two thirds of the orbit and caused 8 mm proptosis, without any disturbance of vision The ophthalmic artery was pushed backwards by the cyst, augmenting the tortuuosity of the branches (Figure 5)

Case 5 Multiple pathological vessels are shown in a 68 years old woman who had unilateral exophthalmos and pulsating supra orbital tumour because of metastasis from a hypernephroma (Figure 6)

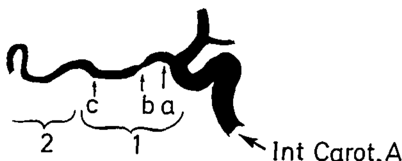
Orbitography may be done with positive or negative contrast media Pneumoorbito tomography, as described by Bertelsen (1956, 1957 1960 1962 and 1966) using air as a negative contrastmedium, is our standard method Tomography is done in lateral and frontal position Providing adequate quantity of air is insufflated in the capsula of Tenon, within and outside the muscle cone and correct X ray exposure are used the orbital content is clearly demarcated The negative contrast of air appears dark on an ordinary X ray film representing less radiologic density than the orbital content In lateral position may thus be delineated the eye ball, the optic nerve and the muscle cone In frontal view the eye ball and some of the ocular muscles are demarcated by air in Tenon s capsule Frontal omograms through the muscle cone may produce sections of the optic nerve and the muscles as well A soft tissue shadow in all pictures is seen to wall out the osseous orbit. Space occupying lesions may alter the orbito-pneumotomogram in several ways Dislocations of the normal content, increase in the orbital soft tissue shadow and abnormal content delineated by air The orbital expansion may be ill defined or the shape and size of a tumour may be more or less well defined by the air contrast

Case 6 Glioma in a 5 years-old girl exhibiting proptosis, papilledema and vision 5/15 is demonstrated as a spindle shaped tumour of the optic nerve Figures 7a and b)

Case 7 (same patient as case 4) A great dermoid cyst is delineated by air and the exact localization shape and size of the cyst were known prior to surgery (Figure 8)



(a) Arteriogram Vide text for explanation



(b) Drawing made from the arteriogram

Fig 2
Ophthalmic artery lateral view

the lumen, and an intraorbital portion (c) which is mostly about 10 mm long, being inferior and lateral to the optic nerve

2 The opticolateral segment makes a sharp bend before taking an upward direction After a subsequent turn it runs for a short distance above the optic nerve This turn is not always detectable on the films

3 Then the artery leaves the nerve to enter the medial part of the orbit as the supraoptic segment

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(a) Carotid angiography lateral view



(b) Destruction of sphenoidal wings (arrow)

Fig 3

Extradural aneurysm of carotid siphon



Fig 4
Glioma of optic nerve angiography lateral view Displacement of arteries (arrows)

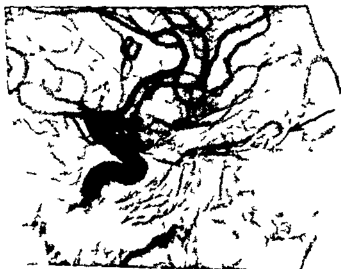


Fig 5
Giant dermoid cyst angiography lateral view Ophthalmic artery pushed backwards. (arrow)



Fig 6

Metastatic hypernephroma selective arteriography of external carotid artery Destruction of bone and pathological vessels (arrows)

Positive contrast orbitography is used as a routine procedure by some (Lombardi 1967) Because of serious accidents reported (Dollfus) we prefer to do supplementary positive contrast medium examinations in cases of reduced vision only, and we have achieved conclusive result by this method when pneumoorbitotomography failed 3 -iodated water soluble contrast medium (Isopaque 260) is mixed with a similar quantity of a local anaesthetic (2 per cent Xylocain) and injected inside the muscle cone as for retrobulbar anaesthesia The position of the needle radiological assured, 3–5 ml of the mixture is injected The cannula is left in position, and because of rapid elimination of contrast medium from the tissue, a few ml of contrast mixture is added during the tomography

Case 8 (same patient as case 3) In the case of a glioma of the optic nerve, the air contrast method was inconclusive The vision being finger counting at 20 cm, the positive contrast method was applied Accidentally the cystlike glioma was punctured and dyed with positive contrast medium (Figure 9a and b)

X ray examinations with contrast media in our opinion are valuable diagnostic aid in the study of orbital tumour We consider no method the



(a) Lateral view



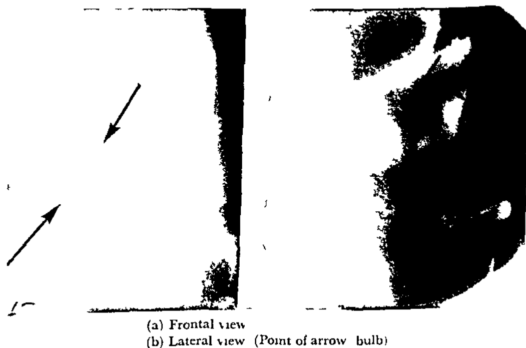
(b) Frontal view

Fig 7
Glioma of optic nerve Orbitopneumotomography

method of choice, and we believe that the use of multiple methods do increase the positive results Orbital phlebography and ophthalmic *angiography can disclose lesions directly* by *showing pathologic vessels* and indirectly by demonstrating vascular displacement By orbitotomography the site and size of space-occupying lesions may be demonstrated The result depends much upon the quality of the X ray films obtained



Fig 8
Dermoid cyst, orbitopneumotomography, lateral view



(a) Frontal view
(b) Lateral view (Point of arrow bulb)

Fig 9
Cystlike glioma of optic nerve (arrows) positive contrast tomogram

Summary

Plain X ray films in orbital tumour may give indicative results and sometimes as in dermoid cysts conclusive results may appear Usually radiologic contrast methods are necessary for the exact and early diagnosis of orbital tumours Orbital phlebography, ophthalmic arteriography, negative and positive contrast-orbitotomography may all supply further information as to the shape size, localization and nature of orbital lesions

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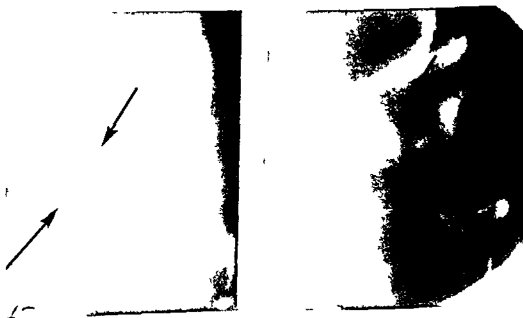
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(a) Frontal view
(b) Lateral view (Point of arrow bulb)

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outside the orbit are not included in this number The table shows the diagnostic distribution of these 17 cases

Hemangioma	3
Optic nerve meningioma	2
Meningioma	1
Mixed *tumour of* lacr gl	1
Neurofibroma	1
Fibroma	1
Dermoid	1
Sarcoid	1
Pseudotumour	1
Fibrosarcoma	2
Osteosarcoma	1
Neurosarcoma	1
Malignant melanoma	1

One notice that 12 benign tumours have been allocated to 8 different histological varieties and 5 malignant ones have been labeled with 4 different diagnoses

The hemangiomas are congenital tumours They have however, a tendency to grow and manifest themselves in adult life The 3 patients represented here were all adults Orbital hemangiomas in children often have a diffuse demarcation and are extremely vascular The method of choice to achieve a definite diagnosis in this age group is therefore considered to be arteriography or venography (Bertelsen 1956) However the cavernous hemangiomas which are found in adults are as a rule, sharply demarcated from the surrounding tissues The vessels are partly thrombosed giving the tumour a firm elastic structure and the blood content and the perfusion rate are often so low that it is hard to diagnose by angiography

In the literature there has been recorded a case where transient hemiplegia arouse from injection of air into an orbital hemangioma (Dollfus 1953) Bottomly & al (1960) have presented a case where a orbital hemangioma was demonstrated by pneumography The 3 hemangiomas in this study have all been demonstrated and diagnosed by pneumotomography without any sorts of complications

Fig 1 is from a woman age 53 who presented with leftsided exophthalmus which had gradually developed over a period of $2^1/_2$ years The frontal view shows a tumourlike shadow above the eyeball and displacing this downwards (Fig 1 A) The tumour is circumscribed by

From the University of Bergen, Department of Ophthalmology Bergen, Norway
(Head Professor Torstein I Bertelren)

ORBITAL PNEUMOTOMOGRAPHY

By

Torstein I Bertelsen

The diagnosis of the deep seated tumours of the orbit will as a rule have to rely upon X ray examinations These examinations will usually have to be aided by some sort of artificial contrast A positiv contrast method may be employed using a radio opaque compound which is injected either intravasculary or directly into the orbital tissues, or a negative contrast is produced by insufflation of air

This paper will summarise the cases of primary orbital tumours which has been treated at the eye department, Haukeland Sykehus, between 1962 and 1968 Special emphasis will be put upon the diagnostic value of orbital pneumotomography

The technical part of this procedure has been delt with in previous papers (Bertelsen 1960, 1962), but I would like to emphasize that relatively large quantities of air (15–20 cc) are required in order to obtain a good result, as a great deal of the air will escape into the eyelids The air has to be deposited in several different positions in the orbit, especially within the capsule of Tenon and inside the muscle funnel but also in the more periferal parts I will also like to stress that reasonable results with this technic cannot be achieved unless the X ray equipment is able to produce serial tomograms where the distance between the sections are 5 mm or less

The diagnosis of an expansive process in the orbit may rest on the fact that the growth either dislocate or deform the normal intraorbital structures as judged by the distribution of the shadows or the air will in fact outline the tumour by distributing itself on the tumour surface Of course this is most often the case when the tumour is demarcated from the surrounding tissues by a capsule

A total number of 5 711 patients were admitted to the eye department in the years 1962–68 17 of these (0,3%) had space occupying lesion in the orbit

Superficial dermoids and a few cases of metastatic deposits from tumours

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Fig 2
Normal optic canals in woman aged 20 with rightsided meningioma of the optic nerve (Fig 3)

Fig 4, 5 and 6 belongs to a 4 year old boy His mother suffered from typical neurofibromathosis Our patient had no skin tumours, but many café au lait spots were noted He presented with a slight rightsided exophthalmus which gradually developed during a quarter of a year and the vision was reduced on this eye to 5/15 Some degree of rightsided papilleoedema was found, while the left eye was completely normal A glioma of the optic nerve was suspected as this is often seen as a complication to neurofibromatosis This type of tumour is considered to expand the optic canal more readily than the meningiomas (Craig & Gogela 1949) In our case the X ray examinations showed that both the optic canals were large (Fig 4) but with insignificant difference between the two sides Pneumotomography (Fig 5) demonstrated a



Fig 3
Pneumotomography in rightsided meningioma of the optic nerve A Frontal section B Sagittal section Arrows points to the thickened optic nerve



Fig 1

Pneumotomography in leftsided orbital hemangioma A Frontal section Arrows points to the tumour The eyeball is displaced downwards B Sagittal section Open arrows outline the tumour The small arrows points to the optic nerve

a thin layer of air The sideview section through the middle of the orbit demonstrates the tumour above and behind the globe (Fig 1 B) The optic nerve is displaced downwards By operation through lateral orbitotomy a circumscribed hemangioma was found, and this was removed without any difficulties

Tumours of the optic nerve are usually benign and they do not affect the very loose connection to the surrounding tissues which are characteristic of the normal nerve Air injected into the capsule of Tenon will easily spread along the surface of the nerve demonstrating any thickening These lesions therefore seems to be the ones which are most easily demonstrated by pneumotomography

Fig 2 and 3 belongs to a 20 year old woman The sight of the right eye gradually subsided to 5/10 during a two year period On examination a relative rightsided exophthalmus amounting to 2 mm was demonstrated Some degree of papilleoedema and marked concentrically decreased visual field were also noted The left eye was completely normal, and a general neurological examination failed to reveal any pathology elsewhere A rightsided meningioma of the optic nerve was suspected, but an X-ray examination of the orbit and the optic canals (Fig 2) were normal A rightsided carotid angiography proved also negative Pneumotomography of the orbit (Fig 3) showed a definitely thickened optic nerve, the thickening extending as far forward as the bulbus The eye and the thickened optic nerve was removed Histological diagnosis was meningioma of the optic nerve

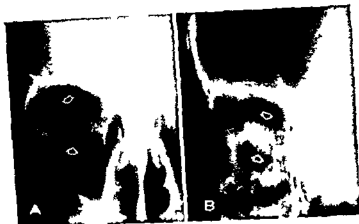


Fig 5

Pneumotomography in rightsided meningioma of the optic nerve A Frontal section B Sagittal section Arrows points to the enormously thickened optic nerve surrounded by air Note that the thickening tapers off both anterior and posterior to a near normal calibre

a 16 year old girl who in a course of two to three years had a gradually increasing exophthalmus and inferior deviation of the left globe X ray examination showed that the left orbital cavity was greatly enlarged upwards A leftsided carotid arteriography showed normal conditions Pneumotomography revealed in the frontal view that most of the upper part of the orbit seemed to be filled with a growth which displaced the bulbus downwards and flattened the upper part of the globe (Fig 7 A) A sagital section through the middle part of the orbit showed the growth above and behind the bulbus (Fig 7 B) It can be seen that the tumour is distinctly separated from the globe and the optic nerve At lateral



Fig 6

Optic nerve meningioma in a boy with neurofibromatosis Left Section showing the optic nerve surrounded by tumour tissue Mallory X 15 Right Tumour tissue x 150 Insertion H P view showing psammoma bodies



Fig 4

Optic canals in a boy aged 4 with neurofibromatosis and rightsided meningioma of the optic nerve (Figs 5 and 6) Both optic canals are large but the difference between them is insignificant

grossly thickened optic nerve both in the frontal and the lateral sections The nerve seemed to have a normal size at the insertion into the bulbus and also in front of the optic canal The nerve with the tumour was removed by lateral orbitotomy Histological examination revealed that the tumour was not a glioma, but a meningioma (Fig 6) The two cut ends showed no tumour cells *

Meningiomas can, however, appear in the orbit without any evident connection to the optic nerve or to the cranial cavity One such case was seen in this study Pneumotomography was not done in this case

The mixed cell tumours will either originate from the lacrymal gland itself or from aberrant lacrymal tissue elsewhere in the orbit The diagnosis of a mixed cell tumour is therefore not precluded by finding a tumour outside the normal site of the lacrymal gland These tumours are usually well defined I have shown in a previous paper that mixed tumours can be demonstrated by pneumotomography, (Bertelsen 1956), which also was the case in the patient included here

Neurofibromas of the orbit may occur as isolated single lesions, or may be part of generalized neurofibromatosis Our case had a solitary tumour Pneumotomography was not carried out, but I have previously proved that such tumours also can be demonstrated by this method (Bertelsen 1960)

Dermoids are ususally superficial tumours, but occationally they may be found deep in the orbit without any appearant connection to superficial structures One such case was seen in our clinic The patient was

* Thanks are due to Ernest Gluck M D Gades Institutt for histological examination of the tumour material

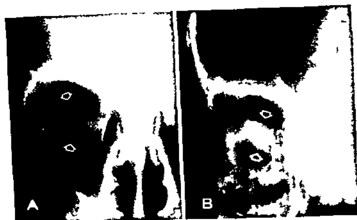


Fig 5
Pneumotomography in rightsided meningioma of the optic nerve A Frontal section B Sagittal section Arrows points to the enormously thickened optic nerve surrounded by air Note that the thickening tapers off both anterior and posterior to a near normal calibre

a 16 year old girl who in a course of two to three years had a gradually increasing exophthalmus and inferior deviation of the left globe X ray examination showed that the left orbital cavity was greatly enlarged upwards A leftsided carotid arteriography showed normal conditions Pneumotomography revealed in the frontal view that most of the upper part of the orbit seemed to be filled with a growth which displaced the bulbus downwards and flattened the upper part of the globe (Fig 7 A) A sagital section through the middle part of the orbit showed the growth above and behind the bulbus (Fig 7 B) It can be seen that the tumour is distinctly separated from the globe and the optic nerve At lateral



Fig 6
Optic nerve meningioma in a boy with neurofibromatosis Left Section showing the optic nerve surrounded by tumour tissue Mallory X 15 Right Tumour tissue x 150 Insertion H P view showing psammoma bodies



Fig 4

Optic canals in a boy aged 4 with neurofibromatosis and rightsided meningioma of the optic nerve (Figs 5 and 6) Both optic canals are large, but the difference between them is insignificant

grossly thickened optic nerve both in the frontal and the lateral sections The nerve seemed to have a normal size at the insertion into the bulbus and also in front of the optic canal The nerve with the tumour was removed by lateral orbitotomy Histological examination revealed that the tumour was not a glioma, but a meningioma (Fig 6) The two cut ends showed no tumour cells *

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Summary

Seventeen out of 5 711 patients (0 3%) referred to the eye department, Haukeland sykehus during a seven year period had primary tumours of the orbit Pneumotomography of the orbit is a valuable and safe method in diagnosing these growths This method gives the best results in benign, encapsulated tumours where the air can spread over the tumours surface Tumours of the optic nerve seems to be the growth which is most easily demonstrated

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Discussion

N Ehlers (*Aa hus*)

At Arhus Kommunehospital we have attempted to diagnose intraorbital tumors by means of arteriography venography and pneumotomography In case of a big tumor the diagnosis is generally easy with small tumores however often difficult

Having observed the paper by Planiol et al (Ann ouil Paris 1967 200 609) on γ-ortography we have used scanning with J[131] albumin and Tc [99m] Positive diagnosis has been obtained with Tc [9m] The method is quick and harmless to the patient

H Gron all (Kristianstad)

During a period of 26 years we have noted and gathered the reports of orbital tumours seen at the eye-department in Kristianstad Hospital This Hospital treated 140 000 patients this period and the hospital serves a population of about ¼ of a million people

The benign tumours were dominated by the dermoid cysts Five of these were found insid the orbit the others presented themselves on the orbital edges

Two cavernous haemangioms were removed through a Kronlein approach with unexpected little bl edings The engorged cavernous cavaties were separated by a connective tissue network infiltrated by round cells

Two tumours were removed through a transfrontal approach by the neurosurgeon One of th se was a two years old girl who had an optic glioma without enlargement of th optic foramen and w thout the cafe au lait skinspots The other case was a 60 years old man who presented with a fibroma with myxomatous degeneration It produced an impression in the o bital roof which could be recognised by X ray examination



Fig 7

Pneumotomography in leftsided orbital dermoid A Frontal section The orbit is enlarged upwards The upper part of the orbit is filled with a soft mass which displace the globe downwards and flattens its upper contour B Sagittal section Open arrows outlines the mass Small arrows points to the optic nerve

orbitotomy one could remove a large dermoid which partly escaped into the temporal fossa through a defect in the lateral wall of the orbit

The diagnosis of *pseudotumour* was made in one single case This concerned a 45 year old man who for three years had pronounced right sided exophthalmus and decreasing vision on this eye Orbital pneumotomography was carried out twice, but it failed to reveal any growth At operation one found a firm, elastic tissue mass with no distinct limitation in the deeper part of the orbit This explains the failure of localisation by pneumotomography

A rapidly increasing exophthalmus without signs of inflammation usually herold a malignant process The four sarcomas in our series all showed this feature If the tumour is infiltrating the surrounding tissue as usually is the case, one would not expect to have much benefit from a pneumotomography All the four cases with sarcomas were children Pneumotomography was not carried out The malignant melanoma was found in a 42 year old woman who for a year and a half had a gradually increasing leftsided exophthalmus The findings on pneumotomography made us suspect a well limited and capsulated tumour in the superior part of the orbit At lateral orbitotomy one found, however, a diffusely limited tumour which could not be removed completely The histological diagnosis turned out to be malignant melanoma One could not demonstrate any connection between this tumour and tissues of the bulbus oculi or conjunctiva Likewise one could not find any other primary tumour Exenteration of the orbit was therefore performed a few days later

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A 52 years old man had a xanthoma at a size of a walnut removed through an orbitomia This intraorbital xanthoma was related to a small skinlesion in the upper eyelid No X ray changes could be demonstrated Histological examination of the specimen showed large fat and foam cells

One meningioma has been found in the orbit who originated from the larger wing of the sphenoid bone, and one from the optic sheeth

A mixed tumour of the lacrymal gland has been removed inside its capsule by a Kronlein operation The patient is still alive and he shows no signs of relapse 12 years after the operation The histological examination showed a benign appearance with epithelial islands in a myxomatous matrix

v Bahr described in 1938 the first case of an orbital Abrikosoffs myoblastomyoma We had a case where the tumour was located near the orbital floor adjacent to the periostium Histological examination of the speciments showed a large syncytium with coarse acidofillic granulations

A very rapid growing pseudotumour was removed three weeks after the first symp toms through an orbitotomia This granuloma was rich in giant cells

Four cases of mucoceles have been recorded

Amongst the malignant tumours one would mention two cases with reticulumcell sarcoma In one case the point of origin was the nasale sinus and in the other the primary focus was located to tissue inside the orbit In the latter case the total exenteration was carried out and in addition a series of X ray treatments were given The tumour de stroyed especially fat and muscle tissues The patient has no sign of recurrence 9 years after the operation

A 66 years old woman was operated on by the Kronlein method and inside the orbit we found a blue black, collapsed tumour and a total orbital evacuation followed The patient died two years after the operation and she had a local recurrence of her malig nant melanoma which grew to the size of a double fist By re examinating the original bulbus one found a very small periferal malignant melanoma in the chorioid with scleral penetration

Two cases of malignant lymfoma tumours have been referred to the radiotherapy department for treatment

A five years old girl was admitted with a shallow tumour under the orbital roof She presented with a severe anemia and changes in the bloodpicture resembling those of an acute myelogenous leucaemia The patient died and a postmortem examination reveiled a green coloured chloroma The histological examination showed the same immature myeloid leucaemic changes as were demonstrated in her spleen and in the bonemarrow

H H Seedorff (Copenhagen)

The contributer points out the advantage of the positive contrast method which has been carried out on 60 patients at Rigshospitalet Copenhagen Two illustrations were shown 1 hygroma from the frontal sinus and 2 tumor of the lacrymal gland

From the University of Bergen School of Medicine Department of Ophthalmology
Head Professor *Torstein I Bertelsen* M D

PRINCIPLES AND SOURCES OF ERROR IN EXOPHTHALMOMETRY A NEW EXOPHTHALMOMETER

By

Martin Davanger

The purpose of exophthalmometry is to produce a numerical measure of the position of the eye in the orbit This measure is used from three different points of view

1 In *absolute* exophthalmometry the result is compared with a known normal value

2 In *comparative* exophthalmometry the results are compared from time to time

3 In *relative* exophthalmometry the result is compared with the measure from the other eye in the same person

Reference points in exophthalmometry

A numerical measure of the position of the eye in the orbit is based upon the definition of two reference points one point on bulbus oculi, and another point on the cranium A measurable relation between the two points must be stated

The natural reference point on the eye ball is apex corneae The other reference point on the cranium has been less evident. Cohn (1865) who constructed the first exophthalmometer used originally the lateral orbital margin as reference It is interesting to note that he later considered this point as frequently assymmetric in relation to an ideal plane vertical through both processus mastoidei This brought him two years later to construct a new exophthalmometer with this the *superior* orbital margin was used as reference (Cohn 1867)

Several other reference points have been proposed (see Drews 1957), but the reference point in general use is still the deepest point on the lateral orbital margin This point will be used as reference in the following

It is important to remember that the exophthalmometric value indicates the relation between *two* points The so-called fixed reference point on the lateral orbital margin may also vary in its position This is prob-

ably an important cause of the wide scatter in the exophthalmometric value found in normal people, from 8 to 24 mm Pathological variations of the position of the lateral orbital margin should be considered both in absolute exophthalmometry (*e g* in anomalies of the cranial growth), in relative exophthalmometry (*e g* in facial assymmetry), and in comparative exophthalmometry (*e g* after fractures and operations influencing the position of the orbital margin)

The simple distance between the two reference points cannot be used as a measure of the position of the eye Most exophthalmometers measure *the distance from apex corneae to a frontal plane through the deepest point on the lateral orbital margin*

In practice there are two different ways of defining this frontal plane, and accordingly we have two different types of exophthalmometers *The first type* is simply a ruler, which alternately is placed on right and left side (Example Luedde's exophthalmometer (Luedde 1938)) This type measures from a frontal plane which is parallel with what must be called ' the facial plane" The frontal plane is placed at discretion

The other type have two rulers which are placed on both sides at the same time (example Hertel's exophthalmometer (Hertel 1905)) With this type is measured with reference to a frontal plane defined by *two* points, namely the deepest point on the lateral orbital margin on right and left side

If the two lateral orbital margins have a symmetrical position, a frontal plane defined according to the first method coincides with a frontal plane after the other definition However, in assymmetry the result of exophthalmometry depends on which one of the two principles has been used This may be of practical importance especially in comparative exophthalmometry

Technical problems in exophthalmometry

In exophthalmometry the following technical problems are faced

1 The zero point of the scale must be placed on the frontal plane described

2 The scale must be held horizontal in a sagital plane

3 Apex corneae must be projected to the scale without parallaxe

4 An exact reading of the projection of apex corneae on the scale must be obtained

We will see how these problems are tackled in some types of exophthalmometers in general use For each point some sources of error will be mentioned

The position of the zero point Some exophthalmometers are simply a modified ruler, and the scale is placed alternatingly on the patient s right and left side In principle, it is quite simple to place the zero point of the

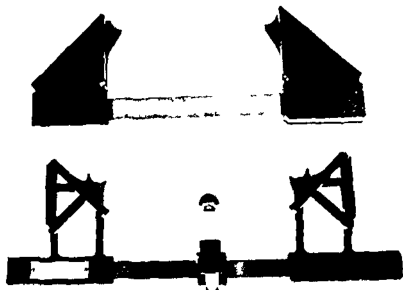


Fig 1
The Hertel exophthalmometer (Keeler) below and a mirror exophthalmometer (Oculus) above

scale in the right position on the lateral orbital margin On the other hand some exophthalmometers of this type are inaccurately made so that the end of the ruler does not represent the zero point of the scale

In the other type of exophthalmometers the Hertel type, in which the scale is placed on both sides at the same time the problem of placing the scale s zero point in the right position is not quite simple The important point is the design of the exophthalmometer s footplate on the lateral orbital margin

Fig 1 shows two widely used exophthalmometers the Hertel exophthalmometer (Keeler s) below and a mirror exophthalmometer made by Oculus above In this connection we are especially interested in the form of the exophthalmometer s footplate on the orbital margin The profile is a circle arc in Oculus exophthalmometer the arc is obliquely set and has a radius of 8 5 mm There is no point on the footplate to show the position corresponding to the zero point on the scale that is where the orbital margin should be placed The position of the orbital margin in the relation to the footplate depends on the distance set between the two halves of the exophthalmometer By using the instrument it will be found that the right distance is not evident to illustrate this the exophthalmometer was set 5 times in succession on the same person, and the

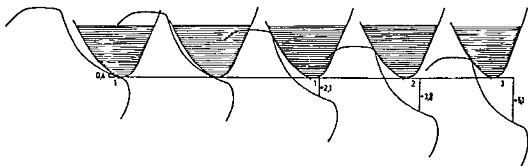


Fig 2
The effect of the position of the exophthalmometer's footplate in relation to the orbital margin

distance varied between 111 and 116 mm The resulting displacement of the footplate in relation to the orbital margin influences the measure to a considerable degree, as can be seen in figure 2 The error caused by the displacement was measured as seen in the figure (the profile of the footplate and a cast of the lateral orbital margin was magnified 10 times in the original figure) It is demonstrated that, *e g* a 2 mm displacement medially will have the effect that the result will be 3,8 mm higher than the correct value

The direction of the scale Exophthalmometers of the Luedde type do not give an adequate solution to the problem of setting the scale in a sagital plane The ruler is placed at discretion, and a certain degree of deviation is probable The reading is supposed to be performed in a direction at a right angle to the scale, and a deviation will introduce an error x which may be calculated (Figure 3) from the equation $x = e - e = a \operatorname{tg} \alpha \cos \alpha \pm (1 - \cos \alpha) e$, where e is the correct exophthalmometric value, e is the value which will be measured when the scale deviates an angle α from the sagittal plane a is the distance from apex corneae to a sagittal

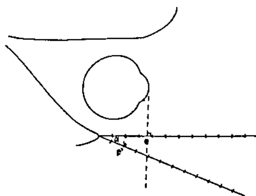


Fig 3
The effect of a deviation of the scale from the sagital plane

plane through lateral orbital margin (the + sign is used when the scale deviates *from* the median plane, the — sign when the scale deviates *towards* the median plane)

The size of the error, as calculated from the equation for some values of e and α is given in table 1 (a = 20 mm (Hertel 1905))

Table 1

e	−10	−5	+5	+10
8mm	+3 4mm	+1 7mm	−1 8mm	−3 6mm
18mm	+3 2mm	+1 7mm	−1 8mm	−3 7mm
28mm	+3 0mm	+1 6mm	−1 8mm	−3 9mm

It will be seen from the table that if the ruler deviates 5° in one reading, and 5 in the other direction in the next reading a difference based on this error of 3,5 mm will be obtained This is of course serious, especially in relative and comparative exophthalmometry

The parallaxe error in exophthalmometry The distance between apex corneae and the scale is at least 15–20 mm, and a right angled projection is then of course decisive

In Luedde s exophthalmometer a projection at a right angle is meant to be obtained by using *two* scales one on each side of the Perspex ruler, which is 8 mm thick When the relevant lines on the two scales coincide the projection should be right

This principle is adequate, but it has been found that the scales are not placed sufficiently accurately on the ruler Seven different Luedde s exophthalmometers have been measured and it was found that the deviation introduced by the relative position of the scales varied between 4 5 and 0 6 The parallaxe error x caused by the deviation may be calculated from the equation $x/b = \text{tg}\,\alpha$ (see Figure 4)

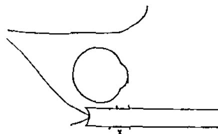


Fig 4

The effect of inaccuracy in the position of the two scales in relation to each other

In table 2 is shown the deviation measured and the resulting calculated error in the exophthalmometric measure for each of the seven exophthalmometers (b=24 mm in 1 position (i e the scale is facing the observer, and b=16 mm in 2 position (i e the scale turns the other way)) The error has also been measured more directly on a simple model, the results of this are also given in table 2

Table 2

	Deviation	Calculated error		Difference	Measured difference
No 1	4,5	+1,87mm	−1,25mm	3,1mm	3,0mm
No 2	3,3	+1,38mm	−0,92mm	2,3mm	2,1mm
No 3	3,0	+1,26mm	−0,84mm	2,1mm	1,7mm
No 4	−2,3	−0,96mm	+0,64mm	1,6mm	2,0mm
No 5	−1,7	−0,70mm	+0,47mm	1,2mm	1,2mm
No 6	1,2	+0,49mm	−0,33mm	0,8mm	0,9mm
No 7	0,6	+0,24mm	−0,16mm	0,4mm	0,1mm

In Hertel's exophthalmometer the problem of parallax is tackled in a peculiar way, which is best understood by analysing the original model, which was described in 1905 (Hertel 1905) The scale is placed in a frontal plane through the patient's temporal region (Figure 5) Cornea is seen in profile by the help of a mirror placed at 45° from the lateral orbital margin By this arrangement apex corneae can be seen projected against the scale If the direction of sight (dotted line in Figure 5 left), deviates from a sagital plane, apex corneae will still be projected against the same point on the scale The condition of this phenomenon is that the

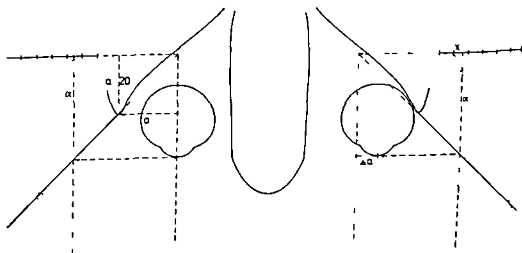


Fig 5
Geometry of the Hertel exophthalmometer

distance between the plane of the scale and the lateral orbital margin is the same as the distance between apex corneae and a sagittal plane through lateral orbital margin Hertel found this last distance to be average 20 mm and constructed his exophthalmometer according to this

For practical reasons he later rejected this construction The scale was now placed laterally on the exophthalmometer and by the help of a mirror *optically* transferred to the original position (Figure 1)

A parallax error may be introduced also in this instrument if the distance between apex corneae and a sagittal plane through lateral orbital margin differs from 20 mm Figure 5, right side, demonstrates this The error x may be calculated from the equation $x = \Delta a \operatorname{tg} \alpha$ Table 3 gives the size of the error for some values of Δa and α

Table 3

α	Δa ±3mm	±6mm
± 5	±0 26mm	±0 53mm
±10	±0 ɔ3mm	±1 06mm

A new exophthalmometer

On the basis of the above analysis, a new exophthalmometer has been constructed in which the sources of error mentioned have been reduced or eliminated The new exophthalmometer is of the Hertel type, that is the footplates of the instrument and the scales, are placed on both sides at the same time

Emphasis have been laid on the design of the instrument s footplate, which is straight not curved and parallel to a frontal plane (Figure 6)

Cornea is seen in profile through a right angled 45 prism The parallax problem is solved by drawing a vertical line on the frontal and the sagittal plane of the prism These lines are placed so that when the lines coincide the sight line is parallel respectively at a right angle to a frontal plane (Figures 6 and 7 left side)

By the help of a screw the prism can be moved along the arm of the exophthalmometer The prism is set in a position where the two vertical coinciding lines of the prism are seen as a tangent to cornea at apex The exophthalmometric value is now given by the position of the vertical line on the sagittal plane of prism along a scale on the arm of the exoph thalmometer By a suitable design this position can be read with a high degree of accuracy

By this construction the parallax error is in principle eliminated It is taken as important that the measurement takes place in two steps First, the instrument is set and afterwards read By this procedure bias is more

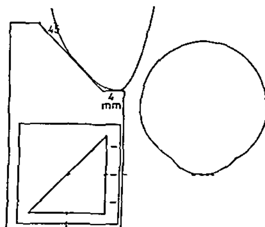


Fig 6
Detail from the new exophthalmometer The footplate, the prism the prism slide and the scale is seen

or less eliminated, the first measurement does not influence the following, and several independent measurements may be performed Thereby the *error may be reduced, and an impression of the accuracy is obtained*

By an addition to the instrument the position of the eye along a vertical and a lateral co ordinate can be measured The reference point on the cranium is the same as in exophthalmometry, and the reference point on the eye is the centre of the pupil A transparent Perspex plate, 8 mm thick, (Figure 7, right side) can be moved by the help of a screw at a right angle to the arm of the exophthalmometer, that is, along a frontal plane Two

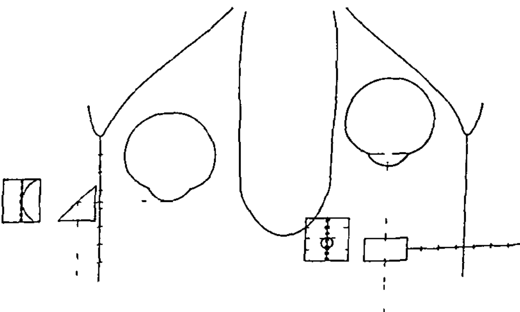


Fig 7
Geometry of the new exophthalmometer

vertical lines are drawn, one on each side of the Perspex plate The parallax error is eliminated when the two vertical lines coincide The Perspex plate is set in a position where the two coinciding lines are projected against the centre of the pupil The position of the plate is read on a scale on the instrument s arm The reading indicates the distance between the pupillary centre and a sagittal plane through the lateral orbital margin

The vertical co ordinate is measured on a scale drawn on both sides of the Perspex plate after the same method as in Luedde s ruler

With this instrument the standard error for exophthalmometry has been found to be 1/3 mm which means that 2/3 of the single measurements lies in the range between the average $\pm$ 1/3 mm

Exophthalmometry has commonly been regarded as an examination with limited value In my opinion this is caused by inaccurate instruments thus the results have not been sufficiently reproducible Measurements with a more accurate exophthalmometer are valuable, especially in comparative exophthalmometry

Summary

Absolute comparative and relative exophthalmometry is defined The concept of reference points is emphasized The exophthalmometric value is defined as the distance from apex corneae to a frontal plane through the deepest point on the lateral orbital margin Technical problems in exophthalmometry are considered under the following headings 1 The position of the zero point 2 The direction of the scale 3 The parallax error

A new exophthalmometer is described

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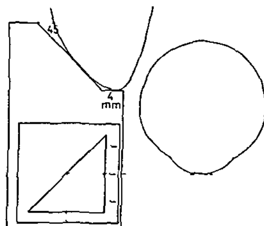


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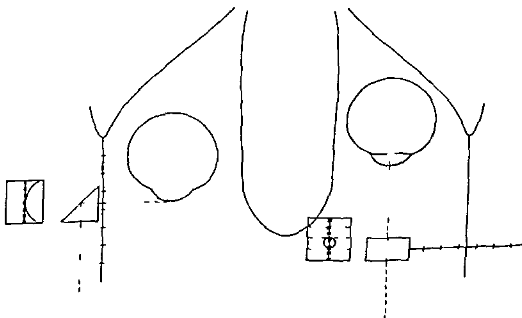


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Geometry of the new exophthalmometer

vertical lines are drawn, one on each side of the Perspex plate The parallax error is eliminated when the two vertical lines coincide The Perspex plate is set in a position where the two coinciding lines are projected against the centre of the pupil The position of the plate is read on a scale on the instrument's arm The reading indicates the distance between the pupillary centre and a sagittal plane through the lateral orbital margin

The vertical co ordinate is measured on a scale drawn on both sides of the Perspex plate after the same method as in Luedde s ruler

With this instrument the standard error for exophthalmometry has been found to be 1/3 mm, which means that 2/3 of the single measurements lies in the range between the average $\pm$ 1/3 mm

Exophthalmometry has commonly been regarded as an examination with limited value In my opinion this is caused by inaccurate instruments, thus the results have not been sufficiently reproducible Measurements with a more accurate exophthalmometer are valuable, especially in comparative exophthalmometry

Summary

Absolute comparative and relative exophthalmometry is defined The concept of reference points is emphasized The exophthalmometric value is defined as the distance from apex corneae to a frontal plane through the deepest point on the lateral orbital margin Technical problems in exophthalmometry are considered under the following headings 1 The position of the zero point 2 The direction of the scale 3 The parallax error

A new exophthalmometer is described

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LONG-TERM PROGNOSIS IN MALIGNANT EXOPHTHALMOS

By

Ruth Ruse

The term malignant exophthalmos embodies the eye symptoms occasion ally encountered in thyro hypophyseal disease exophthalmos, disturb ances of motility, oedema, stasis, optic nerve involvement and corneal ulceration because of exposure, in rare cases complicated by panoph thalmia and destruction of the eyes

The disease may also be called endocrine exophthalmos, endocrine ophthalmopathy, progressive exophthalmos, thyrotropic exophthalmos and thyro hypophyseal syndrome

It is a fairly infrequent disease, usually appearing in the euthyroid patient

Numerous experimental studies have contributed to the elucidation of the pathogenesis (*Horster, Tengroth*) which, however, still remains to be fully clarified

In 1954, *Dobyns* and *Wilson* showed that serum from patients with malignant exophthalmos contains an exophthalmos producing substance formed in the pituitary body, but not identical with thyrotrophin

Furthermore the long acting thyroid stimulator (LATS) exerts an influence It is formed outside the pituitary body and is believed to possess autoimmune properties (*Werner*)

A mucinous oedema is formed in the orbital tissue and in the muscles of the eye (*Wegelius, Asboe Hansen and Lamberg*), and an accumulation of mucopolysaccharides in the skeletal muscles occurs (*Asboe Hansen, Iversen* and *Wichmann*) Increased content in the orbital tissue of gluco proteins has also been demonstrated (*Prame*)

The numerous suggestions for therapeutic measures available, bear witness to therapeutic difficulties in connection with malignant exoph thalmos

General systemic treatment with glucocorticoids causes a regression of the oedema of the orbital tissue and affects an autoimmune process, if

any Favourable results of this treatment have often been seen (*Werner, Lamberg Horster, Macoul* and *Dellaporte, Bonnyns et al Lipman et al*), but some workers doubt the advisability of corticoid treatment, it having been shown that corticoids can aggravate experimental exophthalmos produced by thyrotropin (*Brain*) Furthermore, exophthalmos has developed occasionally in patients after treatment with corticoids for other diseases (*Slansky et al*)

Thyroid extract has been used very extensively (*Brain, Horster*) During recent years favourable results have been reported after treatment with the synthetic D thyroxin (*Horster, Tengroth, Vesterdal*) However, it appears that D thyroxin has not been sufficiently effective in the most severe cases of malignant exophthalmos (*Horster, Green and Farren*)

Treatment with oestrogens has been attempted but with doubtful effect (*V A Jensen Lederer*)

By retrobulbar X ray treatment and retrobulbar injection of steroids or hyaluronidasis, transient and partial remission of the oedema may be obtained (*Horster Kadin Roelsen* and *Skjærbæk Olesen*)

Formerly surgical orbital decompression was a method of treatment frequently suggested (*Naffziger Lyle*) but has now been replaced by medical therapeutics In cases of complications threatening the visual acuity orbital decompression may however still be employed (*Back lund*)

Tarsorrhaphy may be sufficient (*Ehlers*)

Many workers consider malignant exophthalmos to be a self limited disease and this can complicate an evaluation of the effect of treatment However only few studies are available in which patients have been observed over appreciable periods of time Of 24 patients who had been followed for many years *Brain* found 3 cured 10 improved and 11 un changed Similar results were found by *Bardram* who collected 24 cases with an average observation period of three and a half years from the literature

Own material

With the object of elucidating the long term prognosis in malignant exophthalmos a follw up study was carried out of some of the patients who during the period from 1953 to 1963 were checked in the Eye Clinic at the Copenhagen Municipal Hospital

Only severe cases were included

By this procedure the number was limited to 16 3 of those had died and 3 did not appear for examination

Hence the material comprises 10 patients with severe malignant

exophthalmos who were examined after periods of from 5 to 15 years They were 5 females and 5 males, aged 47–77 years

Nine patients were eythyroid at the initial examination One patient presented slightly elevated BMR

In 5 of the patients the eye symptoms appeared after thyroidectomy, in one the disease presented itself in connection with the menopause and in the remaining 4 patients, all males, the disorder set in spontaneously

The diagnosis was established by relating the clinical findings to the results of the laboratory investigations (BMR, serum cholesterol, PBI, T_3 test), X ray examination (orbita, arteriography) and histological examination of skeletal muscles

Table 1

	Visual acuity		Optic atrophy		Venous congestion		Oedema	
	I	II	I	II	I	II	I	II
1	6/12 — 6/60	6/9 — 6/9	—	—	+	—	+	+
2	6/36 — 6/6	6/9 — 6/9	+	+	+	+	—	+
3	6/6 — 6/6	6/6 — 6/6	—	—	+	—	+	+
4	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
5	6/6 — 6/24	6/6 — 6/60	—	—	+	+	+	+
6	6/6 — 6/12	6/6 — 6/6	—	—	—	+	—	—
7	6/24 — 6/18	6/18 — 6/9	+	+	+	—	—	+
8	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
9	6/6 — 6/6	6/6 — 6/6	—	—	+	—	+	—
10	6/6 — 6/6	6/60 — 6/9	—	—	—	—	+	—

During the initial examination, deterioration of visual acuity was found in 5 patients In No 5, the deterioration of visual acuity in the left eye, however, was the result of squint amblyopia In the remaining patients, the deterioration must be regarded as being associated with the current disease All these patients showed improvement of visual acuity at the follow up examination In No 10 the follow up examination revealed senile degeneration of the macula

Two patients presented optic atrophy both at the initial and at the check up examination In both cases the atrophy was unilateral None presented papiloedema

Stasis of the fundus veins and the episcleral vessels diminished during the follow up period The oedema of the eye surroundings and the con junctiva was still present, but no tension of the tissue was observed

Visual field defects were observed initially in two cases (Nos 1 and 2) In both patients the visual field was found to be normal at the follow up

At this time No 7 had developed visual field defect The appearance of the defects varied, from one large defect in both lower quadrants to partial lower temporal quadrant anopsia and bitemporal defect In one case the defect resembled a Bjerrum scotoma Similar defects have been demonstrated by *Hedges* and *Sheie* and *Day* and *Carroll* This is suggestive because *Pohjanpelto* has shown that the intraocular tension in these patients is higher than that found in a normal material

Table 2

	Exophthalmometry		Diplopia		Limitation of movement		Terapy
	I	II	I	I	I	II	
1	26–24	20–20	+	+	+	+	D Thyroxin Hyaluronidase retrobulb
2	28–26	27–25	–	–	+	+	Corticosteroids Tarsorrhaphia Ismelin
3	30–27	23–21	+	+	+	+	Thyreoid extract Corticosteroids
4	21–18	18–17	+	+	+	–	
5	25–19	24–22	–	–	–	+	
6	18–25	25–25	+	+	+	+	Corticosteroids Tarsorrhaphia
7	30–28	32–29	–	–	–	–	Tarsorrhaphia
8	22–18	21–18	+	–	+	+	
9	30–26	normal (un measured)	+	–	+	–	Corticosteroids Thyreoid extract
10	22–22	20–19	+	+	+	+	ACTH Corticosteroids Thyreoid extract

At the follow up study exophthalmos persisted in most of the patients In Nos 4 and 9 the exophthalmos had disappeared (No 9 refused measurement) No 6 was found to have developed bilateral exophthalmos

Diplopia in the primary position and limitation of motility were frequent findings also at the follow up Elevation and abduction were most often affected

At the initial examination, patient No 7 had a keratitis which healed during the follow up period

The therapeutic efforts have been multiple Thyroid extract, D thyroxin glucocorticoids, retrobulbar injection of hyaluronidase and tarsorrhaphia have been employed

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3	6/6 — 6/6	6/6 — 6/6	−	−	+	−	+	+
4	6/6 — 6/6	6/6 — 6/6	−	−	−	−	−	−
5	6/6 — 6/24	6/6 — 6/60	−	−	+	+	+	+
6	6/6 — 6/12	6/6 — 6/6	−	−	−	+	−	−
7	6/24 — 6/18	6/18 — 6/9	+	+	+	−	−	+
8	6/6 — 6/6	6/6 — 6/6	−	−	−	−	−	−
9	6/6 — 6/6	6/6 — 6/6	−	−	+	−	+	−
10	6/6 — 6/6	6/60 — 6/9	−	−	−	−	+	−

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Discussion

E Vesterdal (Copenhagen)

To Dr Ruse s paper on the long term prognosis of malignant exophthalmos I should like to add a few remarks and submit a short survey on the symptoms, signs and therapeutic results in a material from the Finsen Institute Copenhagen from the period 1959–1969 Since in this hospital the isotope department the surgical department and the department of general medicine have taken particular interest in thyroid diseases numerous patients are being referred to us especially patients who have been unsuccessfully treated elsewhere I shall not deal with the ordinary — I might say uncomplicated — exophthalmos but *only with cases that may be designated as post* thyrotoxic exophthalmos or malignant exophthalmos for which Dr Ruse employs the following diagnostic criteria

Palpebral and orbital oedema exophthalmos episcleral venous congestion and in more serious cases chemosis disturbances of motility with pareses of the ocular muscles due to infiltration in and around the muscle fibres, and lastly a closure defect resulting in keratitis etc No mention will be made of the various theories concerning a pituitary thyroid imbalance EPS LATS etc

During th named 10-year period an ophthalmological diagnosis of this disease was made in 51 persons but 6 have to be excluded from the material because they were not treated (either because they died or were discharged to distant parts of Denmark)

Conclusion

The course of disease was roughly identical in the 10 patients followed up

The results of the follow up study give rise to the following comments

During the stage of culmination, malignant exophthalmos causes much discomfort and anxiety to the patient and requires treatment Consequently, only few patients have not been treated, employing two or more of the measures described in the foregoing

However, we can only suppose that the disease is self limited, with a protracted course lasting for months or years An ascending phase is succeeded by culmination at individually varying stages, characterized by stasis and tissue infiltration which seems to incarcerate the bulbus Then follows a descending phase, with a diminishing of the congestion and gradual normalization of the density of the periocular tissue, accompanied by a feeling of improvement being experienced by the patient

The exophthalmos persists and, of course, it will give rise to cosmetic problems, whereas the disturbances of motility will also persist and will cause much complaint on rare occasions only

Only palliative treatment can be offered Critical phases will, presumably, best be alleviated by means of short term intensive steroid treatment (*e g*, 150 mg prednisone daily)

It is extremely important to explain, in comforting terms, the normal course of the disease to the patient

Summary

The long term prognosis in malignant exophthalmos is elucidated by a follow up study after 5 15 years in 10 patients with severe symptoms

It is concluded that the disease is self limited After periods of months or years, some remission may occur, followed by a stationary stage, characterized by exophthalmos and disturbances of motility

During critical phases, brief treatment with large doses of steroids is recommended

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The follow up periods range from 9 months to 9 years averaging 4½ years. All the patients were examined by me in the spring of 1969

In 19 cases the *treatment* was discontinued more than 6 months ago without there having been any recurrences The others are still being treated

Table 3 shows that disturbances of motility with diplopia were *found* in 27 out of the 45 patients i e in 60° As may be seen this did not occur among the patients treated with ^{131}I iodide In 23 the motility had returned to normal at the time of the follow up examination while in 4 there has been no remission Out of the latter patients 3 have been treated for less than a year

Table 3
Restriction of motility with diplopia

	Before treatm	After treatm
Group I (18)	11	2
Group II (12)	8	2
Group III (6)	0	0
Group IV (9)	8	0
45	27	4

Closure defects of the lids were found in 18 patients when first seen 3 of them had keratitis which was cured *One who was treated before Ismelin was available developed* a corneal macula with impaired vision (6/24) in one eye

One patient had a choked disc but this soon subsided without any secondary atrophy

Tonometry was performed in all cases, but without disclosing glaucoma

The treatment was exclusively medical including local eye drops and ointments

Depending upon the level of metabolism the following treatment schedule was used

Table 4
Treatment of malignant exophthalmos

1 Still hyperthyroid pts.	^{131}I possibly combined with non radioiodide + D thyroxine + Ismelin eyedrops
2 Euthyroid pts.	D-thyroxine + Ismelin eyedrops
3 Hypothyroid pts	L thyroxine + D-thyroxine + Ismelin eyedrops

In addition 3 cases of *severe keratitis* with exophthalmometric readings (Hertel) exceeding 30mm received glucocorticoids and corticotrophin in high doses concurrently with the *other medication*

The remaining 45 patients, 40 women and 5 men, were divided into 4 groups (Table 1)

Table 1

Case material

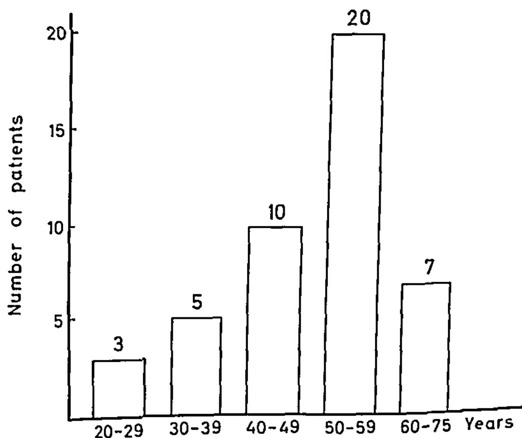
Endocrine exophthalmos (malignant) arising after

Group		No of pts.
I	Thyrotoxicosis treated by thyroidectomy	18
II	Thyrotoxicosis treated by synthetic antithyroid drugs	12
III	Thyrotoxicosis treated by 131 Iodide	6
IV	No history of thyroid disease	9
	Total	45

36 had a history of thyrotoxicosis and the exophthalmos had not developed until anti thyrotoxic therapy had been instituted In 9 cases there was no history of thyroid disease

Table 2 gives the age distribution The majority were between 40 and 60 years of age Only 7 of the women had not entered the menopause at the onset of the disease

Table 2



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In addition 3 cases of severe keratitis with exophthalmometric readings (Hertel) exceeding 30mm received glucocorticoids and corticotrophin in high doses concurrently with the other medication

In two cases lower doses of steroids were administered because of co existing diseases but this proved to aggravate the orbital tension

As already mentioned, no form of surgery was used, neither operations to relieve orbital tension, tarsorrhaphy, nor operations on the ocular muscles

After the advent of Ismelin eye drops, a 5% guanethidine solution from Ciba, we have had no problems on account of lagophthalmos and closure defects The exophthalmos persisted in most cases, but in practically all considerably diminished, depending upon how early the treatment was instituted The average diminution was 3mm and the result was most favourable in the predominantly unilateral types

Lagophthalmos, palpebral oedema orbital tension, episcleral venous congestion, etc. subsided and as already mentioned motility was restored in the majority of cases

I quite agree with Dr Riise that malignant exophthalmos runs a self limiting course, so that treatment should be instituted primarily during crises to counteract complications deleterious to the eye

But I feel, also on the basis of the somewhat more optimistic results mentioned here to day, in particular concerning restoration of motility that long term therapy especially with D thyroxine, should be given after the acute phase The effect of D thyroxine is beyond doubt as seen int al from the increase in the exophthalmometric readings when the drug has to be discontinued for purposes of scanning

The difference between D and L thyroxine has been a matter of much discussion We have alternated (in euthyroid subjects) but owing to unfortunate thyrotoxic episodes and cardiac complications with atrial fibrillation on L thyroxine, we returned to D thyroxine

In respect to the clinical diagnosis, let me point out the numerous apparently unilateral cases of endocrine exophthalmos which turn out to be in fact bilateral as exophthalmometric readings in the contralateral eye decrease after the treatment is instituted Frequently, these cases pass through a cycle the contralateral eye becoming for a time the exophthalmic one This was observed in 6 patients

In conclusion it may be said that with the therapeutic aids available at present the ophthalmologist can in close collaboration with the internists treat all cases of malignant exophthalmos without resorting to surgery with an acceptable cosmetic as well as functional result Therefore as Dr Riise said we can console the patients by describing to them the usual course but we must emphasize to them that the treatment has to be continued for a long time

Incidentally, it will probably not be long before current experimental research into malignant exophthalmos yields results that open up a possibility of preventing this ophthalmopathy

Peep Algvere (Stockholm)

An extradural decompression operation of the orbit by resecting a large portion of the lateral wall and of the roof has been recommended as a possible way of treating progressive endocrine exophthalmus which has been resistant to other types of non surgical treatment After the operation one has noticed an improvement of the visual acuity and satisfactory aliviation of the signs of exophthalmus (Ref Backlund E O Acta Ophth 1968 46 535)

H Ehlers (Copenhagen)

The malignant exophthalmus shows certain characteristics

1 Occurs in clinical euthyroide patients
2 Acute manifestation
3 It may be unilateral or it may appear at different times on the two sides

4 *It may produce ocular complications* (optic disc changes visual field defects)

5 The appearance of dark thick episcleral veins

6 The disease regresses very slowly

All these changes can hardly be explained by hormonal changes alone One has to assume that local processes causes stasis and thrombosis In the eye-department at Rigshospitalet Copenhagen we have treated the acute cases with local manipulation compression anticoagulation and diuretica

T Bertelsen (*Bergen*)

The pressure in the orbit is normally approx 35mm H_2O and seldom rises to values higher than 60mm H_2O In the cranial cavity the pressure is often 150mm H_2O How can it then be possible to increase the volume of the orbit at the expense of the cranial cavity by Naffziger s operation?

From the Eye Department (Heads *B Lauætz* and *H H Seedorff*), Department of Neuroradiology (Heads *H H Jacobsen* and *J Lester*), and Department of Neurosurgery (Heads *J Rushede*, *K Værnet* and *P Rasmussen*), Rigshospitalet, Tagensvej University of Copenhagen, Denmark

OPTIC GLIOMA
CLINICAL FEATURES AND TREATMENT

By

J Fog, H H Seedorff and K Værnet

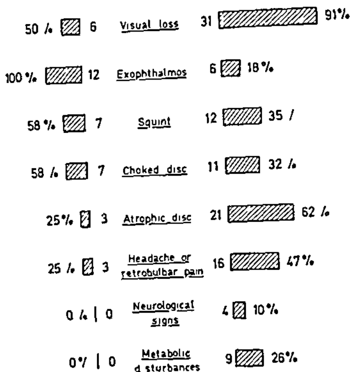
Optic glioma is defined as a benign, slow growing, non metastasizing brain tumour which occurs mostly in childhood (75% before the age of 12 years) It is rare, the incidence having been stated to be 0 8% of intracranial tumours (Martin and Cushing 1923)

One of the first who tried to classify intradural tumours of the optic nerve was von Graefe (1864) Since that time a multitude of papers have been published on primary optic tumours The relationship of primary optic glioma to Recklinghausen s neurofibromatosis (1882) has also been known for almost 100 years It is worth noting that Scandinavian authors have given weighty contributions on this subject, most recently Ehlers (1966), but also Alms (1943), Brændstrup (1944), Godtfredsen (1947), Borberg (1951), and Ladekarl (1964) In his recent paper Ehlers took stock of the subject on the basis of his own studies and the literature Certain authors, *int al* Davis and Byrki, believe that primary optic glioma is only one sign of a disseminated disease and that it *may* represent the first and only sign of Recklinghausen s disease Against this view there is the failure to find histological similarities between optic glioma (arising in glial tissue) and von Recklinghausen's disease (arising in Schwann's cells) Erna Christensen and Ry Andersen (1952) tried classifying the primary cells of optic glioma, but later, like most other workers, gave up this classification Therefore, the more neutral term optic glioma must be kept up for the time being

Figure 1 illustrates schematically the incidence of symptoms and signs in glioma of the optic nerve in relation to the situation of the tumour in the nerve (after Dodge, *et al* 1958)

Present Investigations

As a consequence of the borderline position of the optic nerve between ophthalmology and neurology, a combined assessment of optic glioma



Distribution of patients with glioma restricted to optic nerve and patients with glioma affecting the optic nerve chiasm and optic tract diffusely (46 pts) (After Dodge et al. 1958)

Fig 1

was undertaken from the point of view of the ophthalmological and neuroradiological diagnosis as well as neurosurgical treatment The main problem must be (1) how to diagnose a tumour in the optic nerve as early as possible and (2) how to attack it surgically

Below follow four case reports on patients with optic glioma treated in Rigshospitalet University of Copenhagen within the past few years

In all four cases the clinical ophthalmological signs were unilateral exophthalmos impaired vision choked disc and squinting but no neurological signs were present Other findings and the treatment of the individual patients were as follows

Case 1 A baby aged 6 months with cafe au lait spots on the skin Orbitography showed a tumour in the optic nerve with an enlarged optic foramen (Figure 2) The operation was carried out in two stages first



Fig 2

Case 1 Orbitography Frontal view The circular defect centrally in the contrast medium represents the greatly enlarged optic nerve

intracranial resection of the optic nerve from the foramen to the border of the chiasm, thereafter extradural intraorbital resection of the optic nerve from the globe to the optic foramen Histological diagnosis Glioma of the optic nerve removed in healthy tissue, but with intracranial invasion

Case 2 A child, aged 2½ years, with Recklinghausen's neurofibromatosis X rays showed a normal optic foramen Orbitography Retrobulbar tumour arising in the optic nerve (Figure 3) The operation was performed in two stages, first an extradural procedure on the temporal region, resecting the orbital part of the optic nerve as far as the optic foramen As signs of invasion through the foramen were found, a trans cranial intradural procedure was done later, removing the grossly normal looking nerve as far as the chiasm Histological diagnosis Glioma of the optic nerve right to the last section at the chiasmal border, *i e* non radical removal

Case 3 A child, aged 3½ years, with cafe au lait spots on the skin X rays Enormous enlargement of the optic foramen Orbitography Considerable enlargement of the optic nerve (Figure 4) An intracranial, exploratory operation revealed fusiform swelling of the nerve, with in

vasion of the chiasm and optic tract Histological diagnosis Glioma tissue in the optic nerve Treated by X radiation

Case 4 A child aged 4 years without any signs of Recklinghausen s disease X rays Considerably enlarged optic foramen Orbitography Enormous tumour in the optic nerve (Figure 5 and 6) A transcranial exploratory operation revealed fusiform swelling of nerves with invasion of the chiasm Radical removal was out of the question, and the patient was transferred for X ray therapy

Diagnosis

The four case histories represent even transitions from a tumour restricted to the optic nerve to massive invasion of glioma tissue into the chiasm and optic tract A correct and sufficiently early diagnosis must be based upon the ophthalmological signs (unilateral axial protrusion and choked disc or atrophy) as well as the radiological findings Visual field



Fig 3

Case 2 Orbitography Lateral view The contrast medium has been injected partially subdurally outlining the expanded optic nerve in the posterior part of the orbit. Escape of contrast medium above the sella turcica and on the clivus



Fig 2
Case 1 Orbitography Frontal view The circular defect centrally in the contrast medium represents the greatly enlarged optic nerve

intracranial resection of the optic nerve from the foramen to the border of the chiasm, thereafter extradural intraorbital resection of the optic nerve from the globe to the optic foramen Histological diagnosis Glioma of the optic nerve removed in healthy tissue, but with intracranial invasion

Case 2 A child, aged 2½ years, with Recklinghausen's neurofibromatosis X rays showed a normal optic foramen Orbitography Retrobulbar tumour arising in the optic nerve (Figure 3) The operation was performed in two stages, first an extradural procedure on the temporal region, resecting the orbital part of the optic nerve as far as the optic foramen As signs of invasion through the foramen were found, a transcranial intradural procedure was done later, removing the grossly normal looking nerve as far as the chiasm Histological diagnosis Glioma of the optic nerve right to the last section at the chiasmal border, *i e* non radical removal

Case 3 A child, aged 3½ years, with cafe au lait spots on the skin X rays Enormous enlargement of the optic foramen Orbitography Considerable enlargement of the optic nerve (Figure 4) An intracranial, exploratory operation revealed fusiform swelling of the nerve, with in

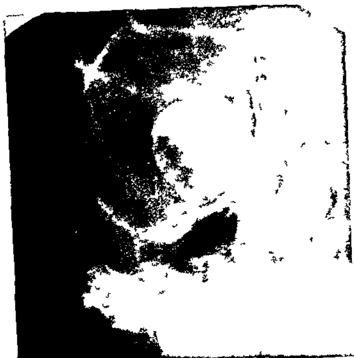


Fig 5
Case 4 Orbitography Frontal view Enormous tumour of the optic nerve The contrast medium surrounds the tumour inside the dural sheath

vein is devoid of risk and well suited for diagnosing retrobulbar tumours but not dependable enough for recognizing tumours of the optic nerve The most important X ray method for this purpose is orbitography At Rigshospitalet University of Copenhagen this study has been done with water soluble contrast medium for the past 6 or 7 years During this period we have carried out 50 studies finding tumours of the optic nerve in 6 including the 4 patients described above We prefer orbitography by positive contrast medium to pneumo orbitography because *In the first place* this affords films of great diagnostic value giving information about expansive lesions, both within and outside the muscle cone with good visualization of the optic nerve *Secondly* tomography is unnecessary and the projections are simple *Thirdly* orbitography by positive contrast is not much of a strain on the patients and may be accomplished within 30 *minutes* We have not observed serious complications apart from one case of transient visual impairment

Pneumo-orbitography as described by Bertelsen (1966), among others carries in our opinion a certain risk Unlike orbitography using positive contrast medium it presupposes tomography in 2 planes and the films



Fig 4

Case 3 Orbitography Optic foramen projection The contrast medium has spread inside the muscle cone The tumour of the optic nerve presents itself as a clear cut defect in the contrast partially overlapping the greatly expanded optic foramen

examination was out of the question, as the patients were too young The radiography may be done by 3 methods

1 General view of the orbit including projections to visualize the optic foramen
2 Orbital venography and arteriography
3 Orbitography using air or water soluble contrast media

A general view of the orbit shows signs of abnormalities in only about 20% of the cases having unilateral exophthalmos Furthermore, the optic foramen is subject to certain anatomical variations, so that an increase of 20% or more in its diameter, as compared with the unaffected side, must be demanded if the appearances are to be interpreted as abnormal, cf Goalwin s (1927) study of 1,000 normal optic foramina only 55% of which were symmetrical Three of our patients had enlargement of the optic foramen according to these criteria Therefore, general views of the orbit are unsatisfactory and carry too much uncertainty to be the only X ray procedure

Orbital venography, performed percutaneously through the frontal

approach it is possible to inspect only the anterior part of the orbit, it hardly ever permits radical excision of retrobulbar tumours, and gives no access to the region of the optic foramen And by this route it is of course, impossible to reach an intracranial extension of an optic glioma

Cushing and Dandy, around 1920 developed the transfrontal approach to the orbit by extradural removal of the orbital roof and the lateral orbital wall This affords a far better view of the orbit, right back to the optic foramen At the same time it is possible to explore the intracanalicular and intracranial part of the optic nerve and chiasm This is of particular importance in optic gliomas where there is no definite possibility of deciding preoperatively whether the tumour is extending through the optic foramen As already mentioned, X ray examination of the optic foramen gives no definite guidance in this respect In one of our patients (Case 2) the optic foramina were normal and equal, and the optic nerve was grossly normal in its intracranial course However, microscopic examination showed tumour cells in the removed optic nerve right to the point of resection at the chiasm In another patient (Case 1) one optic foramen was 5 mm in diameter the other one 7 mm In this case the tumour had spread to the optic canal, but the site of resection at the chiasm showed no signs of neoplastic infiltration

The only means of preventing a glioma in one optic nerve from spreading to the chiasm and thence further is by cutting the optic nerve at the angle of the chiasm (or more correctly 1–2 mm anterior to it) In our opinion therefore this should be done primarily in all cases of optic glioma showing an enlarged optic foramen In other words, these growths should always be approached by the transfrontal route The same applies of course to patients in whom the clinical findings indicate that the tumour has spread to the chiasm or hypothalamus In such cases the problem is a different one Generally there is only a question of exploration and removal of a biopsy in order to decide on the indications for X ray therapy A shunt operation may be considered, if there is a risk of the tumour blocking the foramen of Monro

But in patients without enlargement of the optic foramen and without any clinical evidence of an optic glioma or perhaps even evidence of a tumour situated outside the optic nerve there is a lateral extracranial approach which permits a far better exposure of the orbit and the orbital contents than the classical Kronlein operation

This operation appears to have been described first by Welti in Paris in 1943 but it was developed in several centres independently, as a decompression procedure in malignant exophthalmos It represents the inferior part of the transfrontal operation

From an initial burr hole just behind the zygomatic process of the



Fig 6

Orbitography Lateral view of the same patient as in Fig 5 The tumour is almost spherical The contrast medium in the subdural space is spreading above the sella turcica

are not at all easy to read Moreover, we do not know its diagnostic accuracy

In orbitography with positive contrast medium the diagnostic accuracy has been found to be 80% (Lombardi and Palcerini)

Our orbitographies were performed in the Department of Neuroradiology by experienced radiologists who use the same technique of injecting the contrast medium as in ordinary retrobulbar anaesthesia The situation of the tip of the needle is checked by control films, and thereafter 3 4 ml of a mixture of lidocaine 2% and Urografin 45% is injected Exposures are made immediately in the a–p, lateral, and p–a views The series is repeated at the end of 10 min to show a possibly better distribution of the contrast medium At the end of 20 min the contrast medium has been eliminated This procedure does not give rise to more discomfort than does ordinary retrobulbar anaesthesia

Treatment

The resection of the lateral margin and the anterior part of the lateral orbital wall introduced by Kronlein in 1888, was for many years the classical and only approach to the orbit Through this very limited

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Discussion

O A Jensen (Copenhagen)

It is our experience that gliomas of the optic nerve tend to grow backwards in spite of the limitations of the bony channel In view of this we strongly endorse Dr Seedorff s statement that all methods of examination must be employed in order to clarify the diagnosis as soon as possible If clinical methods have no result an explorative orbitotomy must be performed Otherwise many of these cases very soon become inoperable

Paper read by H H Seedorff before the 19th Scandinavian Ophthalmologist Meeting Bergen 1969

frontal bone, the orbit may be opened From this site, the lateral wall may be removed by a rongeur down to the superior orbital fissure, and practically the entire orbit, including the optic canal, if desired, may be unroofed This affords free access to the entire contents of the muscle cone including the optic nerve If necessary, its intracranial part may be explored also in this or a later stage

This entire subject has been reviewed by Zander and Campiche (1966)

Summary

Orbital tumours, including optic gliomas, make up a typical border line subject between two disciplines in which neurosurgical technique has created a possibility for considerably better and more effective approaches However, the most favourable results are obtained by collaboration between neuro radiologist, neurosurgeon, and ophthalmologist, and an experienced ophthalmic pathologist may prove of invaluable aid, not least in planning possible secondary procedures

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From the Ophthalmic Pathology Laboratory, University of Copenhagen
Head *S Ry Andersen*

MUCOSUBSTANCES OF MIXED LACRIMAL GLAND TUMOURS

Histochemical and histogenetic aspects

By

O A Jensen

BRIEF REPORT

(The full report has been published in *Acta path microbiol scand* Section A *78* 110, 1970)

An earlier histochemical and biochemical examination of the muco substances (MS) of normal human lacrimal glands ([1]) showed an abundance of sialic acid containing MS, but no sulphated MS

The purpose of the present investigation was to apply a battery of histochemical methods to sections of mixed lacrimal gland tumours to determine the pattern of MS and on the basis of the findings to consider the histogenesis

A survey of the *material and methods* may be seen in Table 1

Table 1
Material and Methods

	M	F	Total Number
1942–1967	5	5	10
Age	40–59	13–71	
Recurrences	1	1+2	4
Total material			14 tumours
Fixation	4% buffered neutral formaldehyde/24h/4 C		
Embedding	Routine paraffin technique		
Sections	4μ		

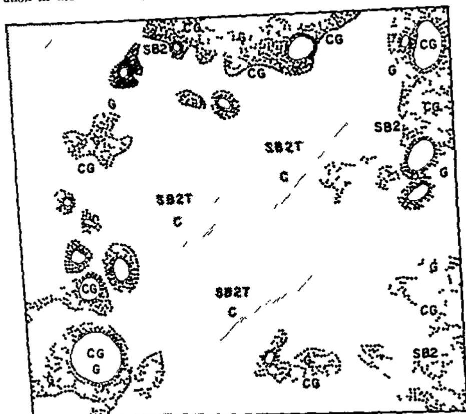
Staining

Periodic acid — Schiff
Metachromatic methods
Alcian blue affinity at different pH and electrolyte conc
Combined staining methods (CI PAS AF AB HID AB)
Fluorescence
Simple protein stains (collagen reticulin elastic tissue)
Blocking reactions
Enzyme digestion

The *results* indicate the presence of the following MS, using the classification of Spicer *et al* (3) modified by Pearse (4)

1 G-mucosubstance
2 C-mucopolysaccharide
3 CG-mucin N±
4 S-mucopolysaccharide B 2 0 T
5 S-mucin B 2 0

The amount and localisation of these substances vary, but the distribution in the material (Fig 1) was mainly such that neutral mucosub



G = G-mucosubstance (Neutral mucosubstances)
C = C mucopolysaccharide (Connective tissue sialomucins)
CG - CG mucin N± (Epithelial sialomucins)
SB2 S-mucin B 2 0 (Epithelial sulphomucins)
SB2T = S mucopolysaccharide B 2 0 T (Connective tissue mucopolysaccharide)

Fig 1

Localisation of the mucosubstances revealed by the histochemical methods. Dots Epithelial strands Grey areas and stippling Interstitial substance

From the Ophthalmic Pathology Laboratory, University of Copenhagen
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Acta Ophthalmologica Vol 48 1970

From the Ophthalmic *Pathology Laboratory* University of Copenhagen
Head *S Ry Andersen*

PRIMARY, HISTOLOGICALLY CONFIRMED ORBITAL TUMOURS IN DENMARK 1943–1962
HISTOPATHOLOGICAL AND PROGNOSTIC STUDIES

By
Poul Eldrup Jorgensen

Read in an abbreviated form to the 19th Meeting of Scandinavian Ophthalmologists, Bergen 18th–21st June, 1969
Aided by a grant from the Danish Anti Cancer League

The present study consisted in an analysis and histopathological classi fication of all primary, histologically confirmed orbital tumours in Den mark from 1943–1962 inclusive This 20 year period was selected as it starts at the time that the card index of the Ophthalmic Pathology Laboratory was established and the year after all malignant tumours in Denmark became notifiable to the Cancer Registry The minimum follow up period is 5 years

Although orbital tumours are fairly rare and the material therefore of modest size I preferred including only histologically confirmed tumours Clinically it is seldom possible to determine the nature of the tumour Therefore all orbital tumours should be studied histologically

These tumours also give rise to differential diagnostic problems, especially in the presence of thyrotoxicosis but mucoceles, metastases tumours from adjacent structure haematomas, thromboses in the sinus cavernosus and orbital inflammations may be confused with true primary orbital tumours

Tumours of the orbit are situated behind the orbital septum and in or within the bony frame of the orbit The distinction from palpebral tumours at the orbital septum is rather arbitrary Therefore some tumours have to be designated as orbito palpebral Such tumours were not in cluded in the present material

Material

The material was collected by perusing the files or case records of large and moderately large eye departments radium centres and neuro-surgical departments Inquiries were made in smaller eye departments

A total of 263 patients are included in the material, which gives an incidence of 0 006% in a population of 4 332 millions

stances (G–mucin) and epithelial sialomucin (CG–mucin N±) were found in the epithelial areas, in the vicinity of these and in the ducts, while connective tissue sialomucins (C–mucopolysaccharide) and hyaluronidase labile connective tissue mucopolysaccharide (S–mucopolysaccharide B 2 0 T) were found interstitially, the latter mainly centrally in the interstitia The epithelial sulphomucins (S–mucin B 2 0), probably derived from the epithelium, were found in the interstitia near the epithelium

This investigation indicates a content of two principally different types of MS in mixed tumours of the lacrimal gland one typical of epithelial MS and the other of connective tissue MS

This finding supports an epithelial and a mesenchymal origin Histochemically one cannot exclude the possibility that the neoplastic epithelium in one way or another can stimulate the normal connective tissue stroma such as to proliferate and produce changes in it There is, however, no evidence of this On the contrary, animal experiments have shown that induction of mixed tumours of the salivary gland by polyoma virus is dependent upon the presence of both epithelium and connective tissue in the gland ([5])

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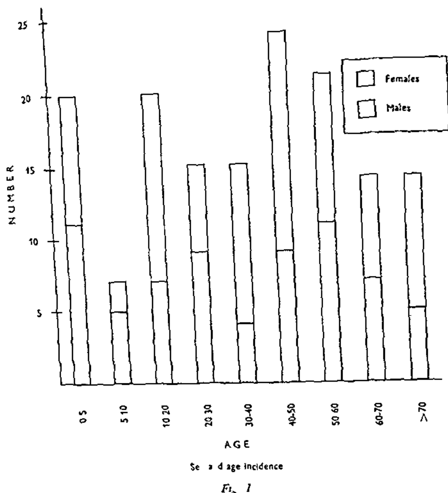
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Se a d age incidence

Fi, *1*

During the first 10 year period 50 cases occurred, while during the latter period there were 100, or twice as many This applies to the benign as well as to the malignant tumours Accordingly the percental distribution of these two groups is the same

This doubling of the incidence cannot be explained solely by the increment in the population which was only 6% But a larger number of tumours are being removed and in particular a larger number are being sent for histological study

Figure 1 gives the age distribution and sex ratio There is no significant sex difference

With the divi ion into 10 year age groups it will be seen that the number of tumours was largest from 0 — 10 years a total of 27 The most common

The number 263 must be considered a minimum of all orbital tumours, as only the histologically confirmed and primary tumours were included Moreover, three had to be excluded because of too poor preparations and deficient data

The histological preparations were procured for all but ten cases for which, however, I have the original histological reports

Frequently new sections had to be cut and special stains employed

The investigation was conducted as a pilot study on 150 patients in alphabetical order

Results

The annual distribution is shown in Table 1 On the average 7–8 cases occurred each year, the minimum being 1 in 1948 and the maximum 16 in 1957

Table 1
Annual Distribution of Orbital Tumours

	Benign			Malignant			
	Male	Female	Total	Male	Female	Total	Total
1943	1	5	6	1	1	2	8
1944	2		2		1	1	3
1945	1	2	3		1	1	4
1946	4	2	6	1		1	7
1947	1	1	2		2	2	4
1948	1		1			0	1
1949	4	1	5	3		3	8
1950	1	2	3	1	2	3	6
1951	1	3	4	1		1	5
1952	2	1	3		1	1	4
1953	1	4	5		2	2	7
1954	1	5	6	3	2	5	11
1955	3		3	2		2	5
1956	2	5	7	5	2	7	14
1957	6	6	12	3	1	4	16
1958	7	1	8	1	2	3	11
1959	5	1	6	4	1	5	11
1960	4	5	9		2	2	11
1961	3	3	6	1	1	2	8
1962	2	3	5		1	1	6
	52	50	102	26	22	48	150

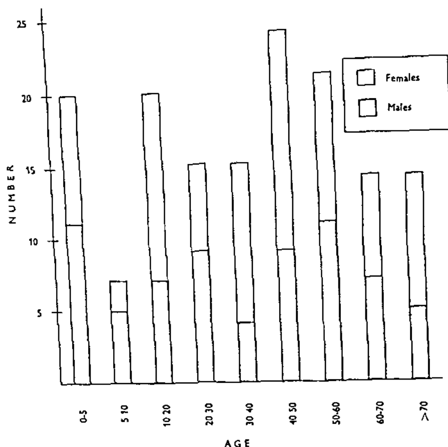


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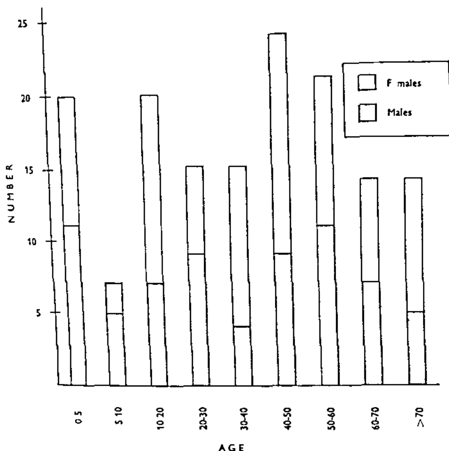
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1948	1		1			0	1
1949	4	1	5	3		3	8
1950	1	2	3	1	2	3	6
1951	1	3	4	1		1	5
1952	2	1	3		1	1	4
1953	1	4	5		2	2	7
1954	1	5	6	3	2	5	11
1955	3		3	2		2	5
1956	2	5	7	5	2	7	14
1957	6	6	12	3	1	4	16
1958	7	1	8	1	2	3	11
1959	5	1	6	4	1	5	11
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tumours in this age group were dermoid cysts and gliomas of the optic nerve, each of which made up 22%

A relatively large number of tumours occurred also in the age groups 40–50 and 50–60 in which particularly pseudotumours were predominant, making up 40% and almost 30% respectively

In all other age groups the distribution of the various types is more even

Table 2
Distribution of Orbital Tumours

	Benign	Malignant	Total	Per cent
Right	38	21	59	40
Left	62	20	82	54
Bilateral	2	7	9	6
Total	102	48	150	100

Table 2 lists the distribution of tumours in the right and left orbit It shows a larger number of benign tumours in the left orbit I am unable to say whether this is accidental The malignant tumours were equally distributed 6% were bilateral, and of the bilateral tumours three quarters were malignant, especially sympathicoblastomas and the group of lymphosarcomas leukaemia

The orbit was divided into the space inside the muscle cone and the space outside The latter was sub divided into 4 quadrants The localization of the tumours is shown in Table 3 The most common site was supero temporal where almost two fifths were situated Out of these tumours more than one third were malignant, consisting mainly of malignant lacrimal gland tumours

The upper nasal quadrant housed about one quarter, one fifth of which were malignant The least common sites were the lower quadrants, the lower temporal quadrant housing 7% and the lower nasal quadrant only 5% In the last mentioned quadrant two fifths of the tumours were malignant

14% of the tumours occupied two quadrants Only 40% of these growths were malignant Only a very few were of diffuse localization

Inside the muscle cone about one tenth of the tumours were situated, and of these almost three quarters were malignant Gliomas predominated, making up 90%

Histopathological Classification

For the histopathological classification I used a modification of Hogan & Zimmermann's (Table 4) The tumours were divided into benign and malignant

Table 3

Localization of Orbital Tumours

	Temporal			Nasal		
Superior	Benign	39	57 = 38%	Benign	28	34 = 23%
	Malignant	18		Malignant	6	
	Benign	10	11 = 7%	Benign	5	8 = 5%
	Malignant	1		Malignant	3	
Inferior						

Double localization	Benign	13	21 = 14%
	Malignant	8	
Diffuse localization	Benign	2	3 = 2%
	Malignant	1	
Inside muscle cone	Benign	5	16 = 11%
	Malignant	11	

The first group within the benign tumours is the choristomas. These tumours are made up of tissue components which are not normally present in the site. Here dermoid cysts predominated.

A hamartoma is tumour like growth of tissue which normally occurs in the site concerned. Within this group *haemangiomas* were common.

However the most common benign tumour was pseudotumour, a total of 29 cases. Together with the dermoid cysts the pseudotumours made up more than half of all the benign tumours.

Benign *mixed tumours* of the lacrimal gland occurred in 4 cases. Out of these tumours three became *transformed* into malignant mixed tumours after the lapse of 4, 10, and 12 years. The *remaining tumour* has not shown signs of malignancy after 11 years follow up.

Within the malignant group gliomas of the optic nerve, lacrimal gland tumours and embryonic sarcomas were most common, comprising together more than half.

Embryonic sarcomas are often called rhabdomyosarcomas, even though no striation is observed, and I doubt whether this designation is correct.

All gliomas of the optic nerve were assigned to malignant tumours. This is perhaps a matter of discussion. Biologically these tumours usually behave as benign but as they all show *invasive growth*, though slow, and as they kill their host if untreated, I prefer to classify them as malignant.

Table 4

Histopathological Classification

	Benign	*Number*	*Malignant*	*Number*
Choristomatous	Dermoid cyst	23		
	Epidermal cyst	1		
	Teratoma	1		
Hamartomatous	Haemangioma	11	Haemangiosarcoma	2
	Sclerosing haemangioma	2		
	Haemangioendothelioma	1		
	Simple cyst	5		
Mesenchymal	Fibroma	2		
	Lipoma	4		
	Myxoma	1	Myxosarcoma	2
	Osteoma	4		
			Embryonal sarcoma	6
			Reticulum cell sarcoma	4
Neurogenic	Schwannoma	7		
	Neurofibroma	5	Neurofibrosarcoma	1
	Meningioma	4		
			Glioma of optic nerve	10
			Sympathicoblastoma	3
Epithelial	Benign mixed tumour of the lacrimal gland	(4)	Malignant mixed tumour of the lacrimal gland	1
		1	3 transformed to Malignant mixed tumour of the lacrimal gland	3
			Adenoid cystic carcinoma of the lacrimal gland	3
			Carcinoma of the lacrimal gland	2
Inflammatory (pseudotumours)	Lymphoma	6		
	Localized inflammatory reaction	23		
Systemic diseases	Sarcoidosis	1		
			Lymphosarcoma-leukaemia	8
			Myelomatosis	1
			Reticuloendothelioses	2
Total		102		48

Sympathicoblastomas were included in the present classification, even though they are not primary This was done because as a rule the first clinical sign of these tumours appears in the orbit, and in most cases the

diagnosis is made on the basis of a biopsy from the orbit It is important, therefore that the ophthalmologist should bear this disease in mind

Within the group of reticuloendothelioses there is one case of Letterer-Siwe s disease and one of disseminated xanthogranulomatosis

Treatment

The treatment of the malignant tumours and the result thereof is apparent from Table 5 The analysis was concluded on 31 12 1967 11 cases were treated by exenteration, some of them combined with radia tion This was used mainly for cases of embryonic sarcoma and lacrimal gland tumours 9 eyes were enucleated usually in combination with extirpation of optic nerve gliomas

Although the material is too small to justify conclusions concerning the most favourable treatment the findings and the impression from the remainder of the material indicate the following For embryonic sar comas and malignant lacrimal gland tumours the prognosis is poor Even a procedure as extensive as exenteration, possibly combined with radia tion does not afford better results than extirpation of the tumour possibly combined with radiation

For gliomas of the optic nerve the prognosis is relatively favourable after extirpation However it is often necessary to perform enucleation as well

The treatment of the group lymphosarcoma leukaemia indicates that radiotherapy alone affords equally good results as radiotherapy combined with operation

Follow up

Table 6 gives the survivals 5 and 10 years after the histological diag nosis Within the 10 year survival time 5 patients had to be excluded because the follow up period was too short

At the end of 5 years two fifths and at the end of 10 years more than half the patients had died of their tumours

Patients with embryonic sarcoma usually succumb within the first couple of years while patients with malignant lacrimal gland tumours survive for a fairly long time At long sight however the prognosis in this group too is poor because of the repeated recurrences of an increasingly malignant nature Within 10 years two thirds of the patients had died of their tumours However a follow up period of 10 years is too short for a final evaluation

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	Osteoma	4		
			Embryonal sarcoma	6
			Reticulum cell sarcoma	4
Neurogenic	Schwannoma	7		
	Neurofibroma	5	Neurofibrosarcoma	1
	Meningioma	4		
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Table 6
Follow-up of the Malignant Tumours

	5 Years				10 Years			
	Number	D f t	D f o c	Alive	Number	D f t	D f o c	Alive
Haemangiosarcoma				2	1			1
Myxosarcoma	2	1		1	1	1		
Embryonal sarcoma	6	4		2	6	5		1
Reticulum cell sarcoma	4	1	2	1	4	2	2	
Neurofibrosarcoma	1			1	0			
Glioma of optic nerve	10	1		9	8	2	1	5
Sympathicoblastoma	3	3			3	3		
Malignant mixed tumour of the lacrimal gland	4			4	4	1		3
Adenoid cystic carcinoma of the lacrimal gland	3	2	1		3	2	1	
Carcinoma of the lacrimal gland	2	1	1		2	1	1	
Lymphosarcoma leukaemia	8	3	1	4	8	5	1	2
Myelomatosis	1	1			1	1		
Reticuloendothelioses	2	2			2	2		
Total	48	19	5	24	43*	25	6	12

Symbols D f t = dead from tumour
D f o c = dead from other cause

* 5 excluded for statistical reasons

Table 5

Therapy and Outcome of the Malignant Orbital Tumours

	Extirpation			Extirpation +Radiation			Exenteration			Exenteration +Radiation			Radiation			Cytostatics			No Treatment		
	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A
Haemangiosarcoma									1		1										
Myxosarcoma						1				1											
Embryonal sarcoma				+1* 1						3		1									
Reticulum cell sarcoma					1								2	1							
Neurofibrosarcoma			1																		
Glioma of optic nerve		1	3 +1	1	1	2													1		
Sympathicoblastoma	1												1			1					
Malignant mixed tumour of the lacrimal gland				1	1				1	1											
Adenoid cystic carcinoma of the lacrimal gland		1		1						1											
Carcinoma of the lacrimal gland													1	1							
Lymphosarcoma-leukaemia	2	1		2									1	1*		1					
Myelomatosis													1								
Reticulo endothelioses										1			1								

Symbols Dt = dead from tumour
Dc = dead f m ot er ca se

* + cyto tat s

From the Eye Clinic Bispebjerg Hospital Copenhagen
Head E Godtfredsen M D

NEURO OPHTHALMOLOGIC FOCAL DIAGNOSIS

By

Erik Godtfredsen

Ophthalmologic signs and symptoms occur at an early stage and are also frequent in patients with intracranial tumours Such have been found in from one half to two thirds of the patients Many patients consult primarily an ophthalmologist with their complaints If choked disc, the chiasmal syndrome, or ophthalmoplegia is found it is up to the ophthal mologist to get started the series of examinations which may result in an adequate diagnosis and therapy As many neuro ophthalmic diseases may threaten both vision and life ophthalmologists become greatly responsible for the welfare of these patients The tasks of the ophthalmologists may be formulated as follows

1 make the diagnosis and after sorting of the patients refer these to special clinics
2 contribute towards focal diagnosis, and
3 follow up the patients to watch them with a view to a suitable remission rate after instituted therapy, give notice in case of recurrence

How often when and how can the ophthalmologist contribute towards a focal diagnosis?

The conditions relating to intracranial tumours being the most important and also those most thoroughly studied there may be reason to concentrate particularly on these

The incidence and the value of localizing the various ophthalmologic symptoms in relation to intracranial tumours will be dealt with first

It is seen in table 1 that although choked disc is an extremely frequent and important cardinal sign of an intracranial tumour it is a highly problematic one where focal diagnosis is concerned This is true of both uni and bilateral choked disc and in the case of Foster Kennedy's syndrome (Wowern)

Conclusion and Summary

Although orbital tumours are relatively uncommon in Denmark, averaging 7 or 8 cases per annum in an average population of about 4 4 millions, these tumours do deserve a great deal of attention

In respect to treatment two factors should be emphasized Although a growth is histologically a benign looking mixed tumour of the lacrimal gland, it should be considered potentially malignant and treated by radical measures (radiotherahy + extirpation + possibly bony resection of the orbital roof), as the study showed that 75% of these tumours underwent malignant transformation in the course of some years

Moreover, it may be impossible to distinguish histologically a benign lymphoma from a lymphosarcoma or an infiltration as a link in lymphatic leukaemia In every case, therefore, relevant clinical studies should be performed to detect systemic disease, and the patient should be closely followed

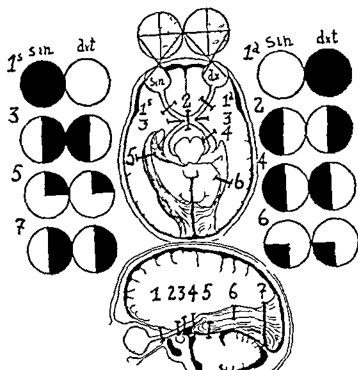


Fig 1
Visual field changes following lesions of different sections of the optic nerve path

lead to tragic mistaken diagnoses (Bardram & Møller, Enoksson) The chiasmatic syndrome accounts for 15 per cent of all visual field defects It is worth pointing out that the differential diagnostic reflections in the presence of atypical chiasmatic syndromes should include simple glaucoma which may occur simultaneously with pituitary tumours (Godtfredsen 1968)

4–7 Lesions of the longest section of the visual path *from the chiasm to* and including *the visual cortex* are associated with a contralateral homonymous hemianopsia the most frequently occurring form of hemianopsia The most important form from a focal diagnostic aspect is the homonymous upper quadrantanopsia which is a typical finding in relation to the temporal lobe tumours being oberserved in one fifth of the patients, according to Edmund s thorough investigations As is well known quadrantanopsia is due to lesion of Meyer s loop the lower and ventral portion of the optic nerve path which winds forwards and round the temporal part of the lateral ventricle The possible diagnostic value of the

Table 1

Frequency and focal diagnostic value of eye signs and symptoms in cases of intracranial tumors

	Frequency	Focal diagnostic value
	in per cent	
Choked disc	60–70	?
visual field defects	40	25
ophthalmoplegias	16	4
pupil anomalies	15	5

Visual field changes, on the other hand, play a very important part On this basis the ophthalmologist can yield weighty focal diagnostic information in 25 per cent of the cases by demonstrating presence of the chiasmal syndrome and homonymous upper quadrantanopsia Ophthalmoplegia of the infranuclear type and pupillary changes each occur in 15 per cent of patients with intracranial tumours, but these are only in a fairly small number (one fourth — one third) of focal diagnostic value, e g in cases of concurrent ophthalmoplegia of the cavernous sinus type Rarer symptoms, such as paralysis of gaze, nystagmus, exophthalmos, each contribute only modestly to a focal diagnosis These symptoms will not be further discussed in this place

Considering all the ophthalmologic signs and symptoms collectively, they can be said to yield focal diagnostic information in about one third of the patients

When and how can the ophthalmologist contribute towards focal diagnosis on the basis of visual field defects?

Fig 1 illustrates in diagrammatic form the correlation between visual field defects and corresponding lesions of the optic nerve path

1 *Optic nerve lesions* with unilateral visual field defects are met with in cases of traumatic optic nerve lesions (Edmund & Godtfredsen) and temporal arteritis, for instance, both with the well known poor prognosis, unlike the conditions relating to retrobulbar neuritis

2 In the presence of *chiasmal affections* ophthalmologists can contribute essentially towards a focal diagnosis, even though the optic chiasm comprises a small section only of the total visual path The chiasmal syndrome, with optic nerve atrophy and bitemporal hemianopsia, is most frequently seen in association with chromophobic pituitary adenomas, which constitute 10 per cent of all intracranial tumours, as well as meningiomas from the tuberculum sellae, and craniopharyngiomas, each representing 2 per cent The two latter tumour forms may be accompanied by atypical chiasmatic syndromes with asymmetric visual fields and running an unpredictable, almost intermittent course, which may

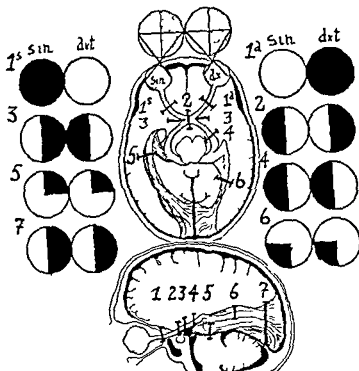


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congruity and macular sparing of the visual fields will not be discussed in this place, the observations made being by no means univocal Reference is made to papers by Enoksson, Huber, Harrington, and Walsh

Significance of ophthalmoplegia in focal diagnosis

Ophthalmoplegia of the infranuclear type occurs more or less frequently in association with the various neuro ophthalmic diseases This symptom is relatively rare in relation to such common diseases as cerebral apoplexy and head injuries (present in 2–10 per cent), whereas more frequent in the comparatively rare diseases, such as intracranial aneurysms (present in 30 per cent, chiefly in the form of oculomotor nerve palsy) As stated, 16 per cent of patients with intracranial tumours present ophthalmo plegia The incidence of this combination is the same in large series of ophthalmoplegia patients Thus, *Rucker* (1958, 1966) found that half of all ophthalmoplegia cases are equally distributed between patients with intracranial tumours, head injuries, and vascular diseases While solitary ophthalmoplegia, with abducens nerve palsy predominating, is of relatively low focal-diagnostic value, combined ophthalmoplegias in the form of a more or less complete cavernous sinus syndrome (ophthalmo plegia and trigeminus I lesion) are of great value Combined ophthalmo plegias are found in from one fourth to one third of patients with intracranial tumours 10 per cent of the pituitary tumours — depending on extrasellar tumour growth — are associated with ophthalmoplegia (Bardram), while in 20 per cent of the patients with malignant naso pharyngeal tumours invading the middle cranial fossa we find a cavernous sinus syndrome (Godtfredsen & Ledermann)

Conversely, in a series of patients with the cavernous sinus syndrome (Jefferson), this is in the same percentages of cases caused by pituitary tumours and nasopharyngeal tumours respectively, as shown in table 2

Table 2

The aetiology in 112 cases of the cavernous sinus syndrome (Jefferson)

Tumors		52 cases
nasopharynx	23	
Pituitary	11	
Aneurysm		38 cases
sacculate	29	
Traumatic		22 cases
carotid fistula	17	

Summary and Conclusion

In patients with neuro ophthalmic diseases especially intracranial tumours, such ophthalmologic signs and symptoms as choked disc, visual field defects and ophthalmoplegia are frequent (*present in 50–60 per cent*) and occur at an early stage

The ophthalmologic symptoms become of focal diagnostic importance in one third of the patients, choked disc and solitary ophthalmoplegia being of no value from a localizing aspect Visual field defects of the type of chiasmal syndrome and homonymous upper quadrantanopsia, as well as combined ophthalmoplegias (the cavernous sinus syndrome) are of great importance in the focal d agnosis The ophthalmologists can con tribute largely towards localizing the tumours situated at the base of the skull, where neuroradiology is a less supreme diagnostic aid

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PUPILLOMOTORIC PERIMETRY IN PSYCHOGENIC DEFECTS OF THE VISUAL FIELDS

By

Paul Enoksson and *Barbro Hallen*

In 1956 Harms presented an extensive study on the possibilities of pupillomotoric perimetry He pointed out that this was of no value in topical diagnosis as all field defects due to organic lesions change the pupillomotoric response irrespective of the location of the lesion He stressed, however, that it could be used for differentiating between organic and functional visual disorders The clinical value of this statement, which does not seem to have attracted the attention it really deserves, is illustrated by the following two cases

Case Reports

Case 1 A K Y, woman aged 23, worked for some time as a nurse and later as technical assistant in X-ray work Four years earlier concussion of the brain and after that several attacks of fainting These disappeared after half a year but reappeared 8 months before the present illness One day when occupied with sorting berries she suddenly reported loss of vision She could, however, move through the room without difficulty After a while she fainted When awake again she complained of headache Eye examination performed the next day A slight temporal defect recorded in the left visual field Five days later admitted to hospital

Examination Uncharacteristic disturbances of coordination

Electroencephalography Unspecific abnormality on the right temporal side

Ocular findings Vision was 1 0 bilaterally Perimetry showed increase of the left visual field defect A restriction of the temporal periphery was recorded combined with an absolute scotoma extending to the left from 5 to 20 degrees from the fixation point

Carotid angiography was performed on both sides and showed no signs of disease The anterior communicating artery and the posterior cerebral arteries did not fill, however

The patient left hospital after three weeks Two months later admitted

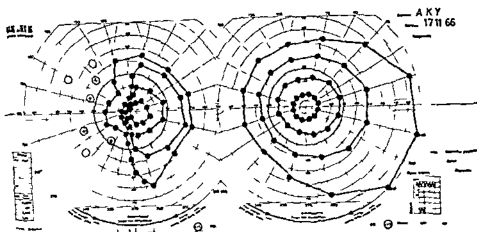


Fig 1

to a neurological clinic after sudden loss of consciousness lasting 5 or 6 minutes Complained of supraorbital pain on the right side

Right carotid angiography performed again This time the anterior communicating artery did fill Suspicion of aneurysm not confirmed At the end of the angiographic procedure the patient reported numbness and weakness on the left side of the body When examined immediately afterwards she appeared to have left sided hemihypaesthesia and almost complete left sided hemiplegia with the exception of the facial muscles

Electroencephalography two days later showed a more pronounced abnormality on the right side than earlier thus indicating the occurrence of brain damage during angiography

Ocular findings Two days after the angiography visual field examination was performed with the perimeter of Goldmann Peripheral left sided restriction was recorded in both fields and with a weak stimulus complete left sided hemianopia was found in the right eye and a left sided para central scotoma in the left A week later the right field appeared normal but the left field showed now almost complete temporal hemianopia Another week later the right field seemed completely normal when studied in detail but the left sided temporal hemianopia persisted (Fig 1) However when the latter finding was controlled by switching on and off the largest and most intense test object in different parts of the left visual field it was observed that it produced pupillary contractions even from points within the defective part of the field As this finding was not compatible with an organic lesion the test was repeated some days later and now in a more systematic way

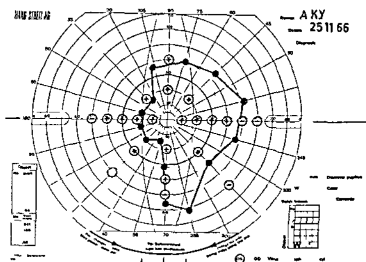


Fig 2

Pupillomotoric perimetry The perimeter of Goldmann was used this time also and with the standardized background illumination The left visual field was first examined with kinetic perimetry A temporal field defect was recorded as before Pupillomotoric perimetry was then performed with the largest and most intense test object The pupillary contractions were symmetrical in all tested meridians, extending to 40 degrees from the fixation point temporally as well as nasally The patient's verbal reports were also recorded (Fig 2)

Course At the time when the pupillomotoric perimetry was performed, the cutaneous sensibility had already turned normal The hemiparesis varied in an unpredictable manner, was not accompanied by any disturbances of peripheral reflexes and disappeared completely within 10 months As the patient did not complain of visual disturbances any more, the visual fields were not re examined

Case 2 A T , girl aged 10 Lost her father in an accident at the age of 2 Had a younger sister and after her mother s second marriage also a half sister When the girl was eight her family moved and she was brought to a new school Soon afterwards she complained of visual deterioration and was allowed to change her seat in the classroom, gradually getting farther and farther forward Her physical development was more rapid than that of her schoolfellows, mammary growth starting at the age of eight and a half This made her feel embarrassed in the other children's company

Ocular findings Right visual acuity 0 1 and did not change with glasses Left visual acuity 0 1 without correction and 0 2 when two spherical

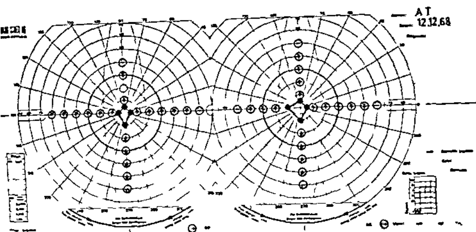


Fig 3

glasses of equal strength but opposite sign was used She could read Jaeger no 3 binocularly Though perimetry showed marked constriction of the visual fields she moved freely at the ward (Fig 3)

Pupillomotoric perimetry This was performed with the same technique as in Case 1 Pupillary contractions were obtained within the field of either eye to a distance of 40 degrees or more from the point of fixation both in vertical and horizontal meridians (Fig 3)

Course The visual disturbance has persisted during an observation time of 6 months During this period menstruations have begun

Comments

The diagnosis of functional neurological disturbances is usually based on indirect evidence This is also true of psychogenic defects of the visual fields When the fields have a spiral form or are extremely constricted though the patient has no orientation difficulties this may be taken as signs of functional disturbance Pupillomotoric perimetry may sometimes prove the functional character of the field defect as in the first of the present two cases The almost complete left temporal hemianopia without any restriction of the right field indicated a lesion of the retina or the optic nerve This could however not be verified at pupillomotoric perimetry Nor did the concentric restriction of the fields in Case 2 appear with this technique This finding may suggest bilateral lesions of the intracerebral visual pathway though this diagnosis seems improbable

The sensitivity of the pupillomotoric response varies widely in different individuals but is usually high at early ages when psychogenic visual

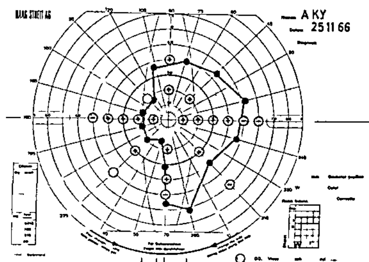


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THE SHAPE OF VISUAL FIELDS IN NORMAL SUBJECTS

By

K Egge

To be published in Acta Ophthalmologica

disorders are prone to appear The present study shows that the instrument of Goldmann may be convenient for pupillomotoric perimetry when used with its standardized background illumination

Summary

Two cases are described, illustrating the value of pupillomotoric perimetry when psychogenic field defects are suspected, and showing that the perimeter of Goldmann is well suited for this technique

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Discussion

G von Bahr (Uppsala)

When evaluating the pupillary reaction after light stimulation of a blind part of the visual field one has to bear in mind that the macula area has a much greater pupillomotoric sensitivity than the rest of the retina Light rays deflected from the lens substance and from the retina itself may therefore produce a pupillary reaction even if the light has been focused and directed against a blind spot of the retina When doing these tests one therefore has to insure a constant macular illumination the same way as *it is done with the hemikinesimeter*

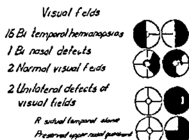
P Enoksson

As no pupillary contraction appeared when the test object was projected within the blind spot scattered light from peripheral parts of the eye ground to the macular region cannot explain the findings

Only 11 patients had pneumo encephalography performed preopera tively One might wonder that only half of the patients had a pneumo encephalography performed as it is known that especially the structures related to the chiasma are shown very clearly by this method, when it is performed with midline laminography using horizontal radiation

However, after hormone examinations, roentgenograms of sella, ophthalmo-neurologic examination and cerebral angiography the indica tions for craniotomy were so evident that a pneumo encephalography was not found necessary in all patients

All patients had an ophthalmo neurologic examination performed pre-operatively and the visual fields were found as follows



Thus five of 21 patients had visual fields differing from the classic bitemporal defect of chromophobe adenoma of the pituitary gland, a defect *Chamlin Davidoff & Feiring*[3] reported in 96 per cent of all cases

One female showed a binasal defect in the visual fields as shown in Fig 1 In the same patient a bilateral excavation of the optic discs forced us to attempt the diagnosis of glaucoma sine tensione as all glaucoma provocation tests were negative

X ray of sella turcica and the angiography were normal Also no signs of dyscrine function were demonstrated But a pneumo encephalography performed later suggested suprasellar tumour and the operation revealed a large chromophobe adenoma

Roentgenograms of the two patients with normal visual fields showed a rather enlarged sella turcica Carotis angiography showed displacement of the internal carotid as well as an elevation of the first part of the anterior cerebral artery

In the patient with a residual temporal island of one eye and a normal visual field of the other eye a similarly enlarged sella turcica was found Moreover angiography showed suprasellar growth with displacement of the internal carotid and also of the anterior cerebral artery

The patient with a preserved upper nasal quadrant on one side and a

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From Odense County and City Hospital, Neurosurgical Department
Chiefs *J Husby, M D , J Overgaard, M D* and *E Marcussen M D*

CHIASMAL VISUAL FIELDS

By

P M Møller and O Hvid Hansen

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Chiasmal Visual Fields

The misinterpreting of chiasmal diseases is very likely to occur, but the possibility of correct diagnosis is however large if one takes the advantages of the many methods of investigation at disposal of ophthalmologists, physicians and neuroradiologists

In Scandinavia this has been emphasized in reports by *Larsson & Nord,*[11] *Bardram & H U Møller,*[2] *Hyllested & P M Møller*[9]

Studying the chiasmal syndrome one is constantly surprised by new aspects of the symptomatology

In Odense we examined records of patients with verified chromophobe adenoma with suprasellar extension, and we tried to correlate the results of the ophthalmologic examinations with the neurosurgical findings by operation and by neuroradiology

The material is small, but rather surprising, justifying the following discussion of certain factors in the pathogenesis of the defects in the visual fields

Material

The material includes 21 patients, aged 15–73 years Twelve had symptoms of disturbed pituitary gland function

All patients had X ray examination of the skull performed and in all except one an enlarged sella turcica was demonstrated

Preoperatively a unilateral carotis angiography was performed in 18 patients, and in three cases bilateral examination was done The angiography was mainly performed for estimating the position of the vessels in relation to the tumour, chiefly for surgical reasons But furthermore reliable signs of a suprasellar space occupying lesion were found in 15 patients

2 The subsequent inferior bitemporal defect is caused by the growing tumour and the chiasmal displacement against the anterior communicating artery

Kearns & Rucker[10] interestingly showed in their study comprising four patients with typical arcuate visual defects of nerve lesion type that the defects were caused by chromophobe adenoma Three of these patients had atrophic discs and one had normal optic nerves All patients had an enlarged sella turcica

These authors cannot exactly explain the development of the defects, but perhaps even ordinary bitemporal defects have more of a vascular basis than is usually supposed, and are not altogether due to direct mechanical pressure

In 1962 *Hoyt*[7] published a study in which he in monkeys by destruction of the papillo macular bundle with photocoagulation was able to follow the course of these special fibers through the optic nerve and the chiasma He concluded, that the lower arcuate bundle is located laterally and inferiorly in the optic nerve and uncrossed fibers of the lower arcuate bundle remained inferiorly and laterally in the chiasma The superior arcuate bundle enters the chiasma superiorly and laterally The structure of the chiasma is almost identical in the anthropoid ape and in man

From his great knowledge of the chiasmal vascular supply and its variability *Hughes*[8] cannot explain the defects in the visual fields as only based on vascular lesions

Francois & Neetens[4] who especially investigated the optic nerve and the chiasmal vascular structure are more inclined to explain that the view field loss is nearly always due to the mechanical effect of compression rather than to vascular obstruction

Discussion

For two reasons we also are most inclined to explain the defects in the visual fields as being caused by mechanical compression of the nerve fibers in the optic nerve and in the chiasma

1 The classic bitemporal defect is related to a tumour the location of which naturally may explain the visual defect
2 The nerve fibers of the optic nerve should be regarded as ordinary myelinized fibers losing their conductibility during a variable period if exposed to pressure Compression of short duration of the chiasma in a patient with chromophobe adenoma may lead to uni or bilateral amaurosis Postoperatively we have experienced full recovery of vision and of visual fields This would not be possible if a loss of vision of this extent was caused by a total vascular obstruction

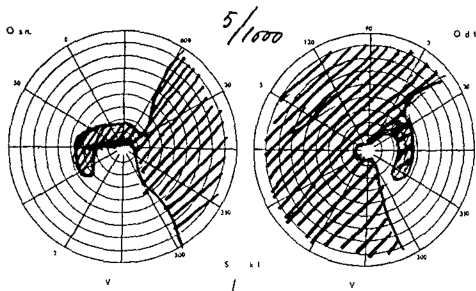


Fig 1

normal visual field on the other is not a frequent finding, however, not extremely infrequent either (*Hughes*[8])

If these five patients are compared with the patients with typical bitemporal visual defects, it is, through our examinations and operative findings, obviously difficult to explain the large variation in the defects in the visual fields, and it is still more difficult to explain their development

Literature

H U Møller[10] reported a case of binasal visual defects and excavated optic discs in a patient with normal tension, in whom operation revealed a chordoma from clivus Blumenbachii

Francois[5] reviewed the literature and found 49 cases of binasal visual defects and reported further three cases He concluded that a displacement of the third ventricle might displace the optic nerves towards the anterior cerebral arteries and the anterior communicating artery Also a tumour in the region of the pituitary gland might produce a similar compression of the optic nerves, and finally a chiasmal arachnoiditis might cause a similar defect in the visual fields

Hirsch[6] mentioned two phases in the development of the bitemporal hemianopsia

1 The pressure of the tumour upwards against the chiasma produces the initial superior defect



Fig 2

A photo of a chromophobe adenoma with an elevated and distended chiasma surprisingly with normal visual fields

In 1962 *P M Møller* in Danish Society of Ophthalmology reported a patient with bilateral amaurosis caused by compression of the chiasma by a meningeoma from diaphragma sellae The tumour was so small that the chiasma was hardly elevated *Hughes*[8] stated, that the chiasmal vascular supply originated from the anterior cerebral artery and from branches directly from the internal carotid According to the angiography these vessels were normal, and also a normal position of the chiasma was found at operation In this case compression of a fixed chiasma upon a tight diaphragma sellae might explain the visual defect

In our opinion the large nasal defects in the visual fields of nerve lesion type might be explained purely mechanically Operation revealed a highly elevated and tight chiasma with a marked open angle between the optic nerves Due to this the lateral superior and inferior fibers in the optic nerves might be compressed against the optic foramina This hypothesis is in accordance with the findings from the degeneration experiments by *Hoyt* [7] The visual defects of nerve lesion type observed in four patients by *Kearns* & *Rucker* [10] might be explained similarly

Also the reported case of unilateral visual defect with preserved upper nasal quadrant only might be explained according to the experimental study by *Hoyt* [7] In this case the pressure may elevate one of the optic nerves medially against the solid margin of the optic foramina

We have no explanation of the exceptional case of a unilateral residual temporal insular visual field

Traquair[13] mentioned the temporal insular visual field in a case of an otherwise characteristic bitemporal hemianopsia A number of nasal fibers running uncrossed through the chiasma might explain this case, but cannot explain the case reported by us

It is difficult to explain why two of our patients with large supra sellar chromophobe adenomas had no defects of the visual fields when one sees the picture taken during the operation of one of the patients (Fig 2)

The large tumour raises the optic nerves upwards and forwards, and all possibilities to give a purely mechanical defect of the visual field are present

We know that the position of the chiasma varies greatly in relation to the sella turcica both with regards to the location in relation to tuber culum sellae and dorsum sellae and the vertical location of the chiasma relative to the diaphragma sellae

Thus one can visualize a backward displaced high situated chiasma where only a very large tumour would cause pressure on the chiasma resulting in defects of the visual fields for purely mechanical reason

In our opinion the hypothesis of the importance of the vascular ob-



Fig. 2

A photo of a chromophobe adenoma with an elevated and distended chiasma surprisingly with normal visual fields

struction for the development of bitemporal visual defects is not supported by the following reasons

1. Our material *includes* several *patients* with a highly reduced vision, *as for instance* only consisting in finger counts and hand movements *In spite* of a large tumour with marked elevation of the anterior cerebral artery not the least defect of visual fields crossing the midline is demonstrated in these patients In these cases the vessels supplying the anterior part of the chiasma are markedly tight and extended, making obstruction highly possible
2. Should a vascular obstruction be of any *importance*, also the vascular supply to the lateral chiasma fibers should be affected It is hard to believe that only the vessels supplying the medial and the anterior parts of the chiasma should be affected by tumours of huge size
3. According to the frequency of variation of the anterior half of the circulus arteriosus Willisii (*Adachi*[1]) the occurence of bitemporal hemianopsia in 96 per cent of cases with chromophobe adenoma (stated by *Chamlin Davidoff* & *Feiring*[3]) does not at all support a vascular genesis

Summary and conclusion

Twenty one patients with verified chromophobe adenoma of the pituitary gland with suprasellar extension are reported

The visual fields are discussed with special reference to five cases without bitemporal hemianopsia An interesting case of binasal visual defect of nerve lesion type is especially emphasized

It is concluded that most defects in the visual fields can be explained by purely mechanical pressure on the chiasma

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NEURO OPHTHALMOLOGICAL PATIENTS WITH BITEMPORAL HEMIANOPSIA

(Follow up study on etiology)

By

D Ruse

The finding of bitemporal hemianopsia during a neuro ophthalmological examination will always arouse interest because, in many cases, it may involve an operable lesion in the region of the chiasm

However this is not always the case A group of patients with hemianopsia were followed up particular importance being attached to the differential diagnostical difficulties which have been encountered in the patients in whom no cause of visual field defect was revealed initially

Material and methods

The patients were selected from those who during the period 1960–67 were admitted to the neurosurgical and neuromedical departments of the University Clinic Copenhagen and who, during examination in the Eye Clinic were classified as suffering from bitemporal hemianopsia By this procedure the sample will quite evidently be selected because the great majority had been examined by an ophthalmologist prior to admission Hereby visual field defects have been excluded, where other causes could immediately be established

The primary technique applied at the visual field examination was campimetry with a 3 mm white and a 10 mm red test object placed at a distance of 1 metre from the patient s eye In cases of doubt and for the follow up studies a Goldmann *perimeter was also used*

During the above period 128 cases of bitemporal hemianopsia were recorded in 34 of these cases the cause of the visual field defect was disputable and the 34 patients were summoned for follow up study The appearance and development of the visual field defects in the individual disorders will be dealt with only sporadically

Results

The distribution of the diagnoses appears in table 1

Tumours	95
Other diseases in optic chiasm and nerves	13
Anomalies in optic disc and retina	12
Uncertain diagnosis	9
Total	129

The large number of tumours can be explained by the fact that the patients were referred mostly from the neurosurgical department The distribution of the tumours appears in table 2

Pituitary adenoma	75
Craniepharyngeoma	7
Meningeoma	7
Dermoids	2
Oligodendroglioma	1
Angioma	1
Metastatic carcinoma	1
Abscess	1
Total	95

By far the most frequent types of tumour affecting the region of the chiasm are pituitary tumours

The distribution corresponds roughly to that found by other workers

In the figure, two types of bitemporal visual field defects found in association with tumours of the pituitary body are shown bitemporal scotoma and bitemporal depression in the visual field

The 13 cases, in which the defect resulted from other lesions in the chiasm and the optic nerve, are distributed as appears in table 3

Optic atrophy uncertain type	6
Trauma	3
Chiasmal arachnoiditis	2
Multiple sclerosis	2
Total	13

The group optic atrophy without known etiology was found to be inhomogeneous, and the visual field defects were somewhat irregular Two cases with cecocentral scotomas were, presumable, tobacco alcohol

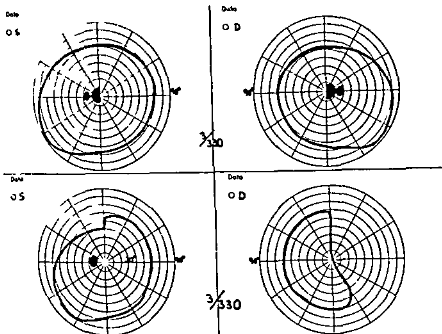


Fig 1
Bitemporal scotoma and bitemporal depression in the visual field in association with pituitary adenomas

amblyopias At the follow up examination some years later, the visual field defects in these two patients had not changed materially Consequently the existence of a tumour is rather unlikely although the possibility of slowly growing meningeoma cannot be excluded completely

In the group of opticochiasmatic arachnoiditis only histologically verified cases are included i e cases in which the optic chiasm has been explored Presumably the incidence of this lesion has previously been over estimated and used as an exclusion diagnosis when no other causes of the bitemporal hemianopsia could be established

During the follow up period two patients developed typical multiple sclerosis

Disorders of the optic disc and the retina will often present difficulties as regards the differential diagnosis even if a diagnosis can be established by ophthalmoscopy The incidence appears from table 4

Ectasia of the fundus	8
Glaucoma	2
Drusen of the optic disc	1
Sectorial pigmentary retinal dystrophy	1
Total	12

Ectasia of the fundus is the most frequent source of error The importance of knowing this differential diagnosis is emphasized by the fact that, in three of these patients, craniotomy and surgical exploration of the chiasm was performed because of the visual field defect

The visual field defects result from localized ectasias in the nasal part of the retina This makes the image of the test object on this part of the retina hazy and consequently, it is not perceived By correction of the vision with minus glasses, the image can become clear, and the scotoma will disappear In these cases the clinical picture is characterized by myopia, astigmatism, moderately impaired vision, inverted vessel emergence on the optic disc and inferior crescent *Bonamour* and *Schmidt* explained this disorder which, in Scandinavia, was described by *Enoksson*, *Odland* and *Riise*

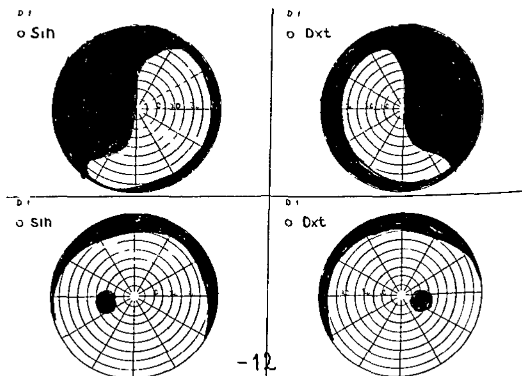


Fig 2

Bitemporal hemianopsia in fundusectasia disappears after correction with minuslenses

In two cases, glaucoma caused the visual field defect, one of them in association with thrombosis of a retinal vein In the other cases, where slight cataract was also present, the visual field defect almost disappeared after mydriasis

In one case the visual field defect was caused, most likely, by drusen in the optic disc Finally, one case of bilateral sectorial pigmentary retinal dystrophy in the nasal part of the retina was found

In 9 cases no explanation of the defects could be established, see table 5

Check up not possible	3
Defects not found at check up	4
Uncertain nature	2
Total	9

The 4 cases which were not found again at check up, are small doubtful defects In one case papilledema was present during the acute stage and the enlarged blind areas were presumably interpreted as being bitemporal hemianopsia

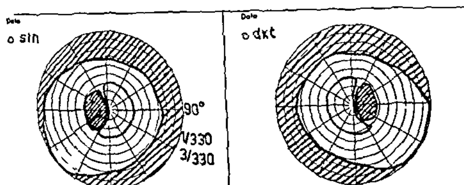


Fig 3
Enlarged blind areas in papilledema simulating bitemporal hemianopsia

The last two cases represented visual field defects for small objects and had remained unchanged for some years without the development of optic atrophy

Conclusion

Reviewing the results it may be said that they correspond roughly to the findings which would be expected in patients with bitemporal hemianopsia seen in a neuro-ophthalmological clinic (*Walsh Traquair, Rucker*) If a patient with bitemporal hemianopsia has reached as far as to a neurologic or neurosurgical department the most likely diagnosis will be pituitary tumour

In cases of doubt exploration of the chiasm has been carried out, in some cases with negative results On the other hand the check ups show that no tumours have been neglected

Atrophy of the optic nerve occurring in some disorders i e multiple sclerosis and trauma may be associated with hemianopsia

Although a number of disorders can be revealed by ophthalmoscopy, they have given rise to differential diagnostical difficulties Of these, nasal fundus ectasias occurred most frequently and were most difficult to distinguish

Summary

Over a 7-year period, 129 patients with bitemporal hemianopsia were encountered in a neuro ophthalmological clinic The majority of these patients had tumours in the region of the chiasm In 34 patients, no exact explanation of the visual field defects could be offered These patients were summoned for follow up study 2–7 years later The results of this study are reviewed

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Discussion

P Kjer (Copenhagen)

I would like to thank dr Riise for his interesting lecture I would however like to bring to your attention the existence of a condition known as hereditary infantile optic atrophy This dominantly inherited disease may in lightly affected cases only manifest itself by the presence of centro coecal scotoms The heavily affected cases however shows a bitemporal bundel defect scotoma which can be confused with bitemporal quadrant anopsia Dr Riise mentioned six cases where the etiology was uncertain and one of these had a centro coecal scotoma A closer examination of the pedegry and family history of patients like this might elucidate the diagnosis

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A MODIFIED PIEZO ELECTRICAL INSTRUMENT FOR OCULOSPHYGMOGRAPHY

By

H G Bynke, M D and *R Öhman, Eng*

A piezo electrical instrument for graphic recording of the corneal pulse has been introduced by *Bynke & Krakau (1964)* This instrument has been demonstrated by *Bynke (1966, 1968)* and *Jensen (1968)* to be suitable for screening diagnosis of unilateral carotid occlusive disease where the amplitude of the corneal pulse wave is as a rule, less ipsilaterally than contralaterally

The original instrument has certain disadvantages The piezo electrical crystal is suspended in a plastic holder which is attached to a frame of balsa wood During the examination the instrument hangs free on the bulb with one leg of the frame behind the head of the recumbent patient so that its centre of gravity lies beneath the contact surface on the cornea (see Bynke & Krakau 1964 Fig 1) The patient must therefore be placed on an examination table with his head on a head rest If he is bedridden this is inconvenient since he has to be lifted from his bed for the oculo sphygmography

On the basis of experiments on rabbits *Bynke (1969)* concluded that in carotid obstruction a light instrument would be expected to produce a larger side difference of the pulse amplitude than a heavy one Consequently there were reasons to try to reduce the weight of the instrument, which is 20 grams

Another drawback of the method is the crystal s sensitivity to high frequencies Small ocular movements blinkings and other mechanical vibrations may disturb the shape of the recorded pulse curve so that measurements of the amplitude may be difficult in some cases In order to improve the instrument some slight modifications have been performed

The improved instrument

The instrument functions in the same way as the original one, and the piezo-electrical crystal and its plastic holder have not been changed

The main modification consists in a change of the frame of balsa wood



Fig 1
The modified instrument hanging on the eye ball

The plastic holder is balanced by means of two short, vertical legs, one on each side of the head The centre of gravity of the hanging instrument is still beneath the cornea, but since the lower, horizontal leg has been eliminated, the patient may remain lying in his bed at the examination (Fig 1) By diminishing the width and length of the frame, it has also been possible to reduce the weight from 20 grams to 10

In order to reduce the signals caused by high frequency mechanical oscillations, a small capacitor (5600 pF) has been introduced parallel to the output of the crystal This capacitor smoothens the curve but at the same time slightly reduces the amplitude of the pulse waves

As yet, the modified instrument has been used only on a small number of patients, including 6 cases with unilateral carotid obstruction In 5 of these the side difference of the pulse amplitude was found to be larger as recorded by this instrument than by the original one Although the material is small, the results support the mentioned hypothesis that a light instrument is preferable to a heavy one for this diagnosis

Summary

A modified piezo electrical instrument for oculosphygmography has been described This instrument has certain advantages as compared with the original one Above all, it is handier to use on bedridden patients

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Discussion

H Davanger (Oslo)

What is the relation between the weight of measuring instrument and the absolute size of the pulsations? If the weight of the instrument decreases I would imagine that the *size of the pulsations also will decrease In other words* pulsations caused by alteration *of intraocular blood olume will result virtually no pulsations of the unindented cornea*

Are there any analysis elucidating the relation between size of pulsations measured by this method and the alterations in the intraocular bloodvolume?

Bynke (answer to Dr Davanger) Due to deformation of the bulb the pulse amplitude decreases as the weight of the instrument increases In rabbits the pulse volume has been found to be 1—2 cu mm

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Head Professor *Torstein I Bertelsen, MD*

REGISTRATION OF ORBITAL PULSATIONS

By

Martin Davanger

The eye-ball is placed in the aperture of the orbit, and fills most of the opening The periphery of the aperture is closed by the orbital septum

Thus, the bulb may be considered a piston in the anterior part of the orbit The orbital walls are bony and rigid Therefore, volume changes of the content of the orbit will induce changes in the position of the eye ball, a volume increase will push the eye forwards, a decrease will bring it deeper in the orbit

The arteries in the orbit have an increased volume in the systole as compared with the diastole, and there are also pulsations in the veins The variations of the blood volume in the orbit will induce pulse-synchronous forward and backward movements of the piston in the anterior aperture, the eye ball

In some pathological conditions the pulsatory movements of the eye ball are so large that the movements are easily seen and palpated This phenomenon is called exophthalmus pulsans It is said that in 90 per cent of these cases the cause is an arterio venous aneurysm in the cavernous sinus In this condition the orbital veins have arterial blood pressure and pressure variations The orbital veins have much larger volume than the arteries, and their wall is much more distensible Therefore, in arterio venous aneurysm the pulse synchronous variations in the volume of the orbital content are considerably larger than the normal, and the forward and backward movements are consequently larger

Another cause of exophthalmus pulsans is a defect in the bony wall between the orbit and the cranial cavity In these cases the intracranial pulsations will be transmitted to the orbital content and the eye ball Such defects may be congenital, in cases of orbital encephalocele, or may be caused by tumours in this region Typical is a neurofibroma as a manifestation of neurofibromatosis, von Recklinghausen s disease

A third cause of exophthalmus pulsans is highly vascularized orbital tumours This condition may be mistaken for an arteriovenous aneurysm, as it may cause both visible pulsations of the eye ball, and pulse syn

chronous noise by auscultation, a phenomenon which is usually considered as indicating an arteriovenous aneurysm

In diseases of the orbit there are pulsations of any degree, from the small movements of the eye ball found in normal persons, to the large pulsatory movements which may ea ily be *recognized by inspection* and palpation, in which case the term *exophthalmus pulsans is natural*

In the diagnostic evaluation of a case of exophthalmus it may be of value to have a quantitative measure of the size of the orbital pulsations This may give an impression of the vascularization of an eventual orbital tumour, and knowledge of this may be *useful when planning* and preparing an operation

Tuyl (1901) constructed an apparatus for graphical registration of the pulsatory movements of the eye ball in the orbit The apparatus consisted *of a two armed lever*, with one short and one long arm A small concave plate is attached to the short arm and this plate rests upon cornea The long arm has a needle which can write on a sheet The backward and *forward movements of the eye are recorded on this sheet, in a magnification* which is determined by the relation between the long and the short arm of the lever

With this apparatus it was found that the pulsatory movements of the eye *ball in the orbit had a size of 0 01 to 0 02 mm in normal persons*

The pulsations of the orbit have also been recorded by plethysmography Wegner (1930) used a capsule which was fixed air tight to the orbital margin The orbital pulsations induce pressure variations in the air in the capsule and the pressure variations are recorded

This method of course does not allow one to measure the size of the movements of the eye ball in mm Another disadvantage is the difficulty in *adapting the capsule air tight to the orbital margin in all cases*

A new method will now be described by which the orbital pulsations are magnified and recorded by the use of a Schiotz tonometer as a linear transducer

In a mechanical tonometer the movements of the plunger are indicated by the pointer in 20 times magnification By using an electronic tonometer further magnification is obtained, and the movements can be recorded on paper by a recorder as *in tonography*

When using a Schiotz tonometer for the registration of orbital pulsations the tonometer s handle and footplate must be fastened in relation to the cranium *This can be obtained* with the help of Merte s tonometer holder which is constructed as an aid in tonography (Merte 1957) The holder consists of a plate which is attached to the patient s forehead by a band *around the head* To this plate the tonometer can be fastened in any relevant position by a holder *attached to the plate*

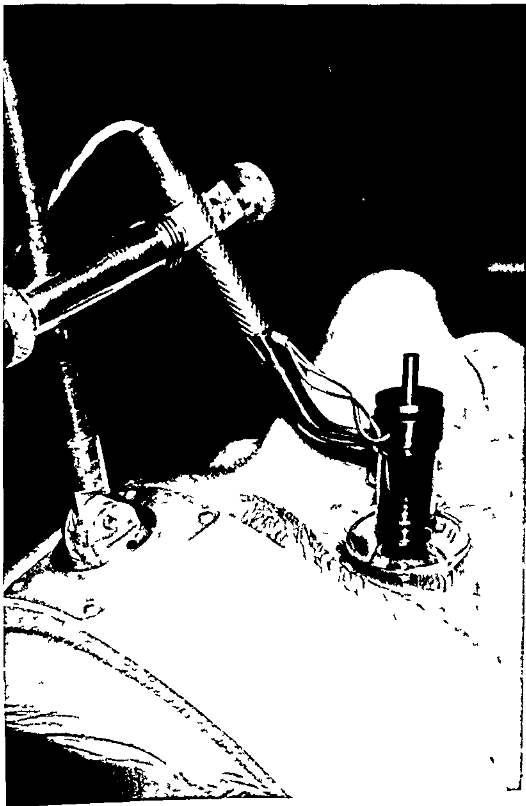


Fig 1
An electronic Schiøtz tonometer held in position by Merté's holder The plunger touches a contact lens on cornea

The patient lies flat on his back (Fig 1) The eye is kept open by a Zeiss l d speculum A contact lens is placed on cornea, I have used + 25 to obtain a sufficiently convex anterior surface The tonometer is lowered until the plunger, and only the plunger, rests upon the contact lens (Fig 2) The footplate should not touch the contact lens

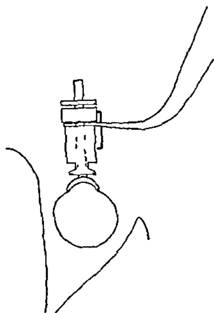


Fig 2
The principle of registration of orbital pulsations by the help of an electronic Schiotz tonometer

The movements of the eye ball are now transmitted via the contact lens to the plunger and thereby recorded by the recorder The size of the pulsations can be measured on the paper and converted into hundredths of millimeter as we know that one scale reading is equivalent to 1/20 or 5/100 mm

In Fig 3 is shown an example of a registration in a normal person The pulsatory movements are in normal cases about 2–3/100 mm and very rarely as much as 5/100 mm

Some registrations demonstrate respiratory movements of the eye in addition to the pulsatory These movements are usually of the same magnitude as the pulsatory

The shape of the pulsations is sometimes different from the rounded waves in Fig 3 The downward waves may have an acute form in others the waves have a less regular complex form as shown in Fig 4 In these

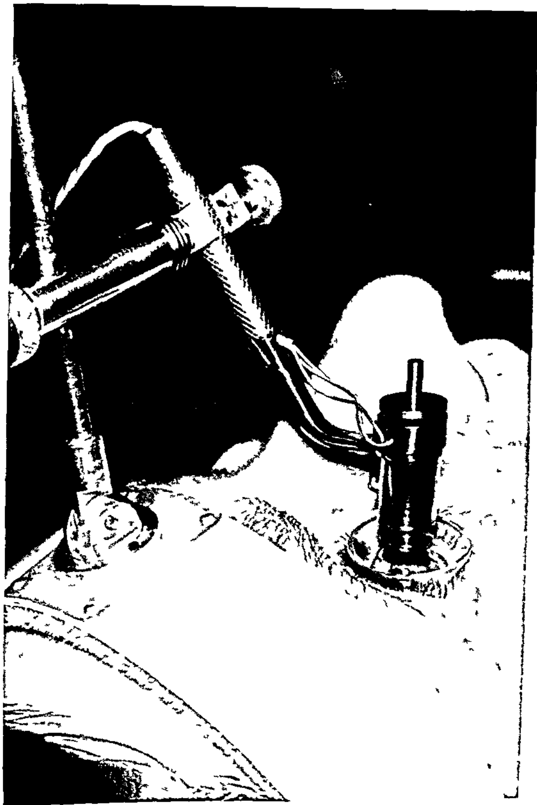


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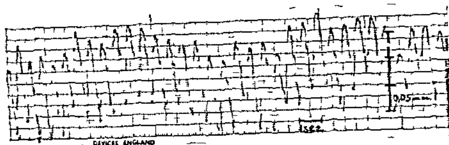


Fig 5
Exophthalmus pulsans

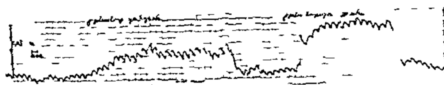


Fig 6
The effect of jugular vein compression

Summary

The pulsatory movements of the eyeball in the orbit are briefly described in normal cases and in exophthalmos pulsans Some methods which have been used in the registration of the orbital pulsations are mentioned A new method is described An electronic Schiotz tonometer is fastened in relation to the head, so that the plunger, and only the plunger rests on a corneal contact lens The tonometer is now used as a linear transducer The pulsatory movements of the eyeball in the orbit are recorded as in tonography Their size is found to be 2–3/100 mm in normal cases Respiratory movements of about the same size are also frequently found Increased and decreased pulsatory movements are registered in some pathological conditions

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Present address Eye Department Rikshospitalet Norway

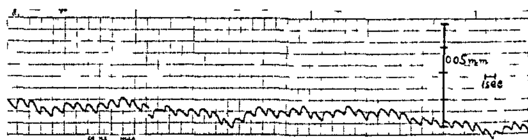


Fig 3
Normal orbital pulsations

cases the shape of the pulsations may be influenced both by the arterial and the venous pulse

Fig 5 shows a curve from a case of moderate exophthalmus pulsans caused by a highly vascularized orbital tumour The pulsations have a magnitude of *slightly less than 1/4 mm, i e about 10 times the normal*

In cases of orbital cellulitis the pulsations have been shown to be pathologically increased

In Fig 6 is demonstrated the effect of jugular vein compression The resulted filling of the orbital veins brings the eye ball markedly forward

The approximate size of the variations of the blood volume in the orbit may be calculated from the registrations of the pulsatory movements of the eyeball We then consider the eyeball together with the orbital septum as a piston in the orbit, 7 cm^2=700 mm^2 in size A movement of *1/100 mm then corresponds to 7 mm^3 volume change* of the orbital content As the normal movements are 2–3/100 mm, we conclude that the normal pulse synchronous variations of the orbital blood volume are about 15–20 mm^3

The method described is recommended to be used as part of the diagnostic evaluation in cases of orbital diseases The result of the registration may be of value in the differential diagnosis, and it may give information concerning the vascularization of an eventual orbital tumour The method has the advantage that very little extra equipment is required A tonograph, a holder for the tonometer, an eye speculum and a contact lens are all that is needed

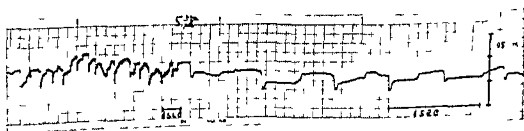


Fig 4
Normal orbital pulsations atypical form

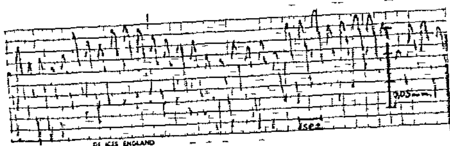


Fig 5
Exophthalmus pulsans

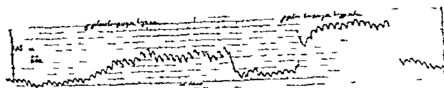


Fig 6
The effect of jugular vein compression

Summary

The pulsatory movements of the eyeball in the orbit are briefly described, in normal cases and in exophthalmos pulsans Some methods which have been used in the registration of the orbital pulsations are mentioned A new method is described An electronic Schiotz tonometer is fastened in relation to the head, so that the plunger and only the plunger rests on a corneal contact lens The tonometer is now used as a linear transducer The pulsatory movements of the eyeball in the orbit are recorded as in tonography Their size is found to be 2–3/100 mm in normal cases Respiratory movements of about the same size are also frequently found Increased and decreased pulsatory movements are registered in some pathological conditions

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OPHTHALMODYNAMOMETRY IN APOPLECTIC PATIENTS WITH HEMISPHERICAL INFARCTION OR TRANSITORY HEMISPHERICAL SYMPTOMS

By

Poul Kjer, M Eiken and *F von Wowern*

Interest in diagnosis of carotid artery disease has been considerable during the recent years The reason may first of all be that in clinical as well as in autopsy materials an essential number of cases have been found with occlusion or stenosis of the internal carotid artery as the specific cause or contributing factor in cerebral vascular insufficiency In large autopsy materials it has thus been demonstrated that stenosis or occlusion of the internal carotid artery occur in about 20 per cent of patients with cerebro vascular diseases[7], and similar findings are reported in angio graphic materials[3] Next the increased interest in diagnosing carotid occlusion and stenosis may be found in the great development that has taken place during the last ten years in vascular surgery New therapeuti cal methods have thus become possible and in suitable cases vascular surgery may be performed on the occluded or stenosed vessels of the neck in order to reestablish blood circulation or to remove the source of the emboli ([1] [6]) In this connection it is of great importance that about 40 per cent of the patients with permanent symptoms of hemispherical infarction before the vascular catastrophe have had transient episodes of neurological deficit from the same hemisphere or amaurosis fugax

Clinically it is impossible to decide whether a cerebral infarction is caused by an occlusion of the internal carotid artery or the middle cerebral artery and it is practically impossible and also unreasonable to carry out arteriography on all patients with cerebral apoplexy Using technically less difficult methods of examination it could be possible to select those patients for angiography who are suitable for vascular surgery Theoretically ophthalmodynamometry ([8] [1] [16]) or related methods as oculosphygmography ([4] [5] [9]) seem suitable as an introductory procedure being technically practicable and harmless in order to compare the haemodynamic conditions on the two sides The drawback of the method

is that an occlusion of the internal carotid artery cannot be excluded if the pressure is the same on both sides as the collateral circulation can maintain a normal pressure in the retinal arteries on the same side as the carotid occlusion

Arteriography however should be performed on all patients who have only had transitory ischaemic attacks

Material and methods

Through a team work with all the departments at Gentolte Hospital we have attempted to do neurological examination and history to carry out arteriography, electroencephalography ophthalmodynamometry and carotid echography in *all* patients admitted to the hospital with symptoms of hemispherical infarction or transitory ischaemic attacks but with particular interest being paid to the patients with cerebro-vascular symptoms suggesting a disease in the arteries of the neck. No attempt of selection has been made and we have tried as much as possible to carry out the above mentioned examinations on all apoplectic patients referred to the hospital Several patients however have not been registered either because they died before the examination programme could be carried through or on account of the general condition being too poor or other diseases giving contraindication to the examinations

All the patients (123 cases) had one or more arteriographies of the common carotid artery, on one or both sides and about one third of the cases (43 patients) had also aorto cervical arteriography by the method of Seldinger In this examination a tube is introduced in the ascending aorta after punctuation of one of the big arteries of the extremities and contrast is injected through the tube In this way the large neck arteries are reproduced in their full length from the arch of aorta to the base of the skull

The purpose of the present study was to correlate the results of arteriography with the results of ophthalmodynamometry and to draw attention to the value of ophthalmodynamometry in diagnosing carotid occlusion and stenosis A pressure difference of 25 *per cent or more* between the two eyes was considered as a positive finding

A preliminary report on the results of the examination in the first 42 patients has been published previously[18] The complete study is not finished yet The present material consists of a total of 123 patients 104 of whom had hemispherical infarction and 19 only transitory ischaemic attacks (table 1) The distribution of age and sex is also seen in the table

In the age group under 40 years there was a total of 7 patients (5 women and 2 men) 2 of the women (30 and 35 years old) with hemispherical infarction had taken oral contraceptives and arteriography

showed respectively occlusion of the middle cerebral artery and the internal carotid artery

A total of 67 patients had accompanying cardio vascular diseases (the numbers in brackets)

TABLE 1

THE PATIENT GROUP

AGE	FEMALE	MALE
<40	5(1)	2
40 - 49	2(2)	7(2)
50 - 59	10(2)	23(11)
60 - 69	15(12)	32(21)
>70	16(8)	11(8)
	48(25)	75(42)

HEMISPHERICAL INFARCTIONS	104
TRANSITORY ISCHEMIC ATTACKS (HEMISPHERICAL)	19
TOTAL	123

Results

It has been connected with certain difficulties in finding a system for the results of angiography In stenosis of the carotid artery for instance not only the degree and the extension of the stenosis have to be considered but also the degree of the atherosclerosis In an attempt to compare the different findings schematic drawings have been made on the base of the X ray photographs and the angiographic findings have been divided as follows

1 Occlusion
2 Severe stenosis, i e the diameter of the stenosis is less than half of the diameter of the vessel before and after the stenosis
3 Moderate stenosis, i e a diameter larger than half of the diameter of the vessel
4 Severe atherosclerosis, i e a great length of the wall of the vessel is pronounced irregular and angiography does not show any real stenosis

TABLE 2

IMMEDIATE PROGNOSIS 104 COMPLETED STROKES

ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO SCLEROSIS	SEVERE ATHERO-SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN PART	NOR-MAL	TO-TAL
MEAN AGE	62	64	61	64	71	72	46	59	
DEAD		1	1				1	1	4
NO REMISSION	2	1	4	2	2			1	12
CONSIDERABLE REMISSION	4	5	10	4	1	2		11	37
TOTAL REMISSION	12	3	7	2	2			25	51
TOTAL	18	10	22	8	5	2	1	38	104

5 Moderate atherosclerosis

6 Kinking of the carotid artery

7 Normal conditions

Of course this angiographic classification can be criticised and it refers only to the conditions of the internal carotid artery, but not to its branches Here it is necessary to draw attention to the fact that a total of 14 patients in the material had an occlusion of the middle cerebral artery These 14 patients are equally dispersed in all the angiographic groups

The prognosis for the patients with infarction of the hemisphere is of course very variable depending on the basic changes Table 2 illustrates the *clinical condition* of the patients when discharged from the hospital correlated to age and the result of the angiography

The prognosis is relatively better in the group where angiography showed normal conditions in the carotid artery

One patient in this group died however and another had no remission of the paresis Both patients had angiographically verified occlusion of the middle cerebral artery

The clinical carotid symptoms transitory ischaemic attacks ipsilateral headache bruits and the external carotid symptom are of limited diagnostic value (table 3)

The external carotid *symptom* is a visible prominence of one or more branches of the superficial temporal artery on the same side as the occluded internal carotid artery[11] This symptom was only found in two cases

Ophthalmodynamometry was carried out in 112 patients (table 4) A significant difference between the two sides was found in half of the

TABLE 3

CORRELATION OF ANGIOGRAPHY AND CLINICAL SIGNS AND SYMPTOMS

	NUMBER OF PATIENTS							
	20	16	24	11	4	4	2	42
ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO-SCLEROSIS	SEVERE ATHERO-SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN PART	NOR-MAL
TRANSITORY ISCHEMIC ATTACKS	8	11	10	5	1	2	1	9
IPSILATERAL HEADACHE	1		2	3			1	1
BRUITS	7	9	5	2	1		1	2
CAROTIS EXTERNA SYMPT			1					1

patients with severe stenosis and in about 2/3 of the patients with carotid occlusion

In a few cases with no significant difference between the two sides, remarkable low pressure values were found on both sides indicating a bilateral carotid obstruction

Finally it should also be mentioned that a few patients had positive ophthalmodynamometry and angiographically verified occlusion of both carotid arteries

In a total of 11 patients ophthalmodynamometry was not performed on account of diseases in one or both eyes retinal detachment, glaucoma

TABLE 4

CORRELATION OF ANGIOGRAPHY AND OPHTHALMODYNAMOMETRY

	NUMBER OF PATIENTS							
	20	16	24	11	4	4	2	42
ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO SCLEROSIS	SEVERE ATHERO SCLEROSIS	KINKING STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN PART	NOR MAL
OPHTALMODY NAMOMETRY SIGN. REDUCED IPSILAT. SIDE		8	15			1		2
SIGN. REDUCED CONTRALAT SIDE								
INSIGNIFICANT	0	6	8	9	4	3	2	34
NOT DONE		2	1	2				6

TABLE 5

CORRELATION OF ANGIOGRAPHY AND OCULAR SYMPTOMS

	NUMBER OF PATIENTS							
	20	16	24	11	4	4	2	42
ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO SCLEROSIS	SEVERE ATHERO-SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN. PART	NORMAL
TRANSIENT MONOCULAR BLINDNESS	1	3	2			1		1(?)
OCCLUSION OF RETINAL ARTERY		1	2	1				
OCCLUSION OF RETINAL ARTERY WITH CONTRALAT. HOMONYMOUS HEMIANOPSIA		1						
HOMONYMOUS HEMIANOPSIA TRANSIENT				1				1
PERMANENT		4	8	3		1		4
UNILATERAL RETINOPATHY	1	1	2					
PUPIL SMALLER ON AFFECTED SIDE		1		1				1
DIPLOPIA	1	2		1				1
UNEQUAL HYPERTENSIVE VASC CHANGES		1						

with narrow angles cataract and recent embolus in the central retinal artery or its branches Moreover poor cooperation made the examination impossible in a few cases

Neuro-ophthalmological symptoms were found in 38 patients (table 5) Among the transitory ischemic symptoms special attention was paid to the monocular transient loss of vision (amaurosis fugax) which causes some patients to consult their ophthalmologist This symptom however was only mentioned by 7 patients but it has probably been present in several more cases Many of the patients however had aphasia were confused or unconscious on entering the hospital so that the case histories inevitably must be insufficient

Occlusion of the central retinal artery was seen in 5 patients and angiography showed respectively severe stenosis occlusion and moderate atherosclerosis of the internal carotid artery In one of these patients there was moreover contralateral homonymous hemianopsia.

Permanent homonymous *hemianopsia* was present in 20 patients while 2 patients only had transient hemianopsia Many of these patients were

almost unable to cooperate at the examination on account of poor general condition In four cases there was a sparing of the upper quadrant of the defective side of the field

Unilateral retinopathy was seen in 4 patients In this symptom cotton wool patches are seen in the nerve fiber layer of the eye homolateral to the lesion in the internal carotid artery[14] As stated by Hollenhorst[8] these patches are ischemic infarcts produced by hypotension

This unilateral hypotension is probably also the reason for *assymetric hypertensive retinal vascular changes* with less hypertensive changes on the side of the affected carotid artery[10] This symptom was found in one case

Miosis on the affected side was seen in 3 patients and 5 complained of *diplopia*

In addition to the symptoms mentioned in table 5, a few patients had respectively gaze palsy, conjugate deviation, unilateral ptosis, unilateral decreased corneal sensibility and unilateral paresis of the orbicularis oculi muscle

14 patients had vascular surgery Endarterectomy, removal of the thrombus or patch grafting In 6 of these patients there was not 25 per cent difference in the pressure between the two eyes before surgery

In 5 patients with more than 25 per cent difference between the eyes before surgery, the pressures became equal — at any rate in 4 of these patients after surgery There was no follow-up examination of the fifth patient after surgery

In 2 patients the difference between the two eyes was a little less than 25 per cent before surgery and no difference between the eyes after surgery

Finally the examination could not be carried out in one patient

Discussion and conclusion

In the present material consisting of 123 patients with permanent or transitory hemispherical symptoms hemiparesis was the most frequent symptom This was present in 104 cases

All the patients had one or more arteriographies, and in 24 cases occlusion of the internal carotid artery was found, while 16 cases showed severe carotid stenosis 31 cases showed moderate changes of the internal carotid artery either as a slight stenosis (20 cases) or moderate atherosclerosis (11 cases) 4 patients had severe atherosclerosis and 6 patients showed various changes kinking of the internal carotid artery, stenosis of the innominate artery or stenosis of the siphon

42 patients showed normal conditions of the internal carotid artery

The usual clinical symptoms including the neuro ophthalmological carotid symptoms were only of limited value in diagnosing an obstruction of the internal carotid artery

Hollenhorst[8] has stated that the incidence of amaurosis fugax is higher among patients having intermittent insufficiency than among those having thrombosis This is confirmed in the present series but the number of patients with this symptom is rather limited

Regarding the homonymous hemianopsia Walsh[15] has pointed out that often there is a relative sparing of the upper quadrant of the defective side of the field This is ascribed to the fact that the superior portion of the optic radiations is supplied by the middle cerebral artery and the lower portion by the posterior cerebral artery In the present material 4 patients had a lower homonymous quadrantanopsia The angiographic findings in these 4 patients were respectively occlusion severe stenosis and atherosclerosis of the internal carotid artery

As an exact diagnosis is of vital importance for a possible treatment and for the study of the spontaneous course of the cerebrovascular diseases it is obvious that there has been great interest in finding other and simpler methods of examination than arteriography

Ophthalmodynamometry has proved to be useful in a number of cases and in the present material there was positive finding in about half of the cases with severe stenosis and about 2/3 of the cases with occlusion of the internal carotid artery

Weigelin and Lobstein[16] found reduced pressure in 70–80 per cent of the cases with unilateral carotid occlusion

In the present examination a pressure difference of 25 per cent between the two eyes was considered significant (according to Spalter), but other authors ([12] [1]) have considered a difference less than 25 per cent as significant

Ophthalmodynamometry does not render arteriography superfluous, as the moderate stenoses or mural thrombi do not change the haemodynamic conditions to such a degree that they possibly could be disclosed by ophthalmodynamometry The method however is suitable as the first examination in obscure cerebral insults amaurosis fugax unilateral retinopathy hemianopsia and the like

Furthermore a positive ophthalmodynamometry compared with a negative common carotid arteriography indicates the performance of the more comprehensive central arteriography in cases felt to be suitable for surgery

Considering the great interest in diagnosing the cerebrovascular diseases and the increasing therapeutic activity ophthalmodynamometry may in our opinion contribute in essential respects — also to the postoperative follow up of the effect of vascular surgery

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Furthermore a positive ophthalmodynamometry compared with a negative common carotid arteriography indicates the performance of the more comprehensive central arteriography in cases felt to be suitable for surgery

Considering the great interest in diagnosing the cerebrovascular diseases and the increasing therapeutic activity ophthalmodynamometry may in our opinion contribute in essential respects — also to the post operative follow up of the effect of vascular surgery

Summary

The results of ophthalmodynamometry and carotid angiography are compared in 123 apoplectic patients with hemispherical infarction or transitory hemispherical symptoms

Ophthalmodynamometry showed a significant difference between the two sides in half of the patients with severe stenosis of the carotid artery and in about 2/3 of the patients with carotid occlusion The clinical carotid symptoms and especially the neuro ophthalmological symptoms are compared with the results of angiography

14 patients had vascular surgery An account is given of the result of ophthalmodynamometry in these cases

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Discussion

I Hoiven (Oslo)
At the Neurosurgical department in Rikshospitalet Oslo we have had the opportunity to carry out dynamic tonometry when the internal carotid artery was ligated in cases with intracranial aneurisms It was possible to observe the development of collateral circulations from the ipsilateral external carotid artery and from the contralateral internal carotid artery It starts a few hours after the obliteration

In some cases the collateral circulation can be of such a magnitude that tests done months or years afterwards fail to show any differences in the amplitude of the cornea pulsation on the two sides In such long standing cases the dynamic tonometry combined with a compression manoeuvre of the carotid artery may give valuable diagnostic informations

We do agree with dr Bynke to abstain from compression of the carotid artery in acute cases of artery occlusions or stenosis which has resulted in cerebral insults An indiscriminate use of the compression method might endanger the patient by dislodging an arterial thrombus. The acute cases will usually produce a significant difference in the cornea pulsations as measured by dynamic tonometry This will make the compression manoevre superfluous

From Oslo University Eye Department, Rikshospitalet Oslo, Norway
(Head Professor dr med Thore L Thomassen)

DYNAMIC TONOMETRY

IV The corneal indentation pulse in giant cell arteritis

By

Ivar Hørven

Patients suffering from giant cell arteritis may clinically be divided into three groups, those with no eye involvement, which means approximately 50–60 per cent of the cases (*Egge et al 1966, Meadows 1968*), those with symptoms from one eye, and those with symptoms from both eyes The need has been pressing for a safe clinical test by which the immediate danger of eye involvement could be evaluated in these cases This test should be sensitive enough to give a conclusive answer in eyes with a minor decrease in blood supply, a decrease which up to testing time not yet had caused any clinical symptoms

The purpose of the present study is to present dynamic tonometry (*Hørven 1968*) as an easy, accurate and safe clinical test in these cases A test which offers information of diagnostic and, sometimes, of prognostic interest

Material and methods

The study includes all cases of giant cell arteritis which were treated for eye involvement in our department during the period November 1967 –May 1969 Case no 1 was examined with a provisory set up in January 1967 and is also included in the present material There were 10 patients, 8 males and 2 females The age averaged 72 1 years (57–80) and the erythrocyte sedimentation rate (SR) at admittance was elevated in all cases with an average value of 65 3 mm per hour (40–98) Histological examination of a temporal artery biopsy yielded pathological findings typical for giant cell arteritis in all but one of the cases studied, in this one case (Case no 10) no giant cells were found although definite pathological changes were demonstrated in the intima and media of the artery wall including partial disappearance of the internal elastic lamella

Dynamic tonometry was performed at admittance and at various intervals during the period of treatment of the patients in question Due

to summer vacation Case no 6 had the initial dynamic tonometry examination postponed to 11 days following start of treatment The dynamic tonometer is made according to the known principles of electronic tonometers with certain important modifications (*Hørven 1968*) In its present state the tonometer yields an output of 1 mV per 1 μ plunger deflection An output of 50 mV will, therefore, correspond to a plunger movement of 50 μ which equals one scale reading Schiøtz When high sensitivity is employed, the tracings may be kept on the running paper of the recorder by use of a zero suppression unit

The corneal indentation pulse amplitudes as recorded with the dynamic tonometer is normally of the same order of magnitude in the two eyes with an average value of about 30 μ of plunger movement which equals 0 6 scale reading Schiøtz Based on statistical evaluations of the results obtained in 65 subjects the difference in amplitude between the two eyes of the same subject is normally less than 15 per cent (*Hørven 1970*) Thus a pathological result of this test in patients suffering from giant cell arteritis may be defined as follows 1 By demonstration of a decrease in corneal indentation pulse amplitudes of 15 per cent or more in eyes yielding clinical symptoms of the disease 2 By recording corneal indentation pulse amplitudes of less than 13 μ in eyes with or without clinical symptoms A 13 μ corneal pulse amplitude is the lowest value ever recorded in a normal eye (*Hørven 1970*)

Results

The results obtained are summarized in Table 1

A marked decrease in corneal indentation pulse amplitudes was demonstrated in all but one (Case no 6) of the eyes yielding clinical symptoms of giant cell arteritis In the 8 eyes which demonstrated a visual acuity of light perception (l p) or amaurosis at admittance the corneal pulse amplitudes averaged 2 6 μ (0–12) As a rule the decrease in corneal pulse amplitude was more pronounced in the amaurotic eyes although a zero pulse amplitude was recorded in an eye with 5/7 5 in visual acuity (Case no 7)

In Case no 6 a 13 per cent decrease (normal eye 60 μ affected eye 52 μ decrease 8 μ) was demonstrated in the affected eye This decrease is regarded as a possible but not definite pathological finding As mentioned above the initial dynamic tonometry test was performed 11 days following start of treatment in this case which possibly explains why only a minor difference was found

Of the 10 cases studied 3 yielded bilateral symptoms at admittance in hospital 7 offered definite pathological dynamic tonometry test results in both eyes and 1 a possible pathological test result in the 'mate eye'

Table 1

Results obtained in 10 patients suffering from giant cell arteritis

f c = finger counting L p = light perception, am = amaurosis

Case no	Initial corneal pulse amplitude (μ) Right	Initial corneal pulse amplitude (μ) Left	No of eyes with clinical symptoms	No of eyes with positive test result	Visual acuity Initial Right	Visual acuity Initial Left	Visual acuity Final Right	Visual acuity Final Left	Follow up period
1	2	2	2	2	1 m f c	am	6 m f c	am	28 months
2	0	2	1	2	am	5/10	am	5/7 5	10 „
3	20	12	1	1+?	5/10	1 m f c	5/10	5/7 5	15 ,
4	17	37	1	1	2 m f c	5/5	2 m f c	5/5	17 „
5	11	12	2	2	5/30	am	3 m f c	am	6 „
6	60	52	1	?	5/5	5/25	5/5	5/7 5	10
7	1	0	1	2	1 p	5/7 5	am	5/5	2 „
8	10	0	1	2	5/5	1 p	5/5	am	2 ,
9	0	0	2	2	am	am	am	am	1 week
10	12	6	1	2	5/10	am	5/10	am	1 „

?=see text

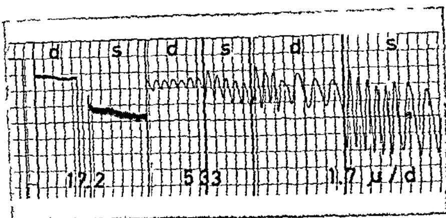


Fig 1

leaving only 2 patients (i e 20 per cent) with monolateral eye involvement This points to a marked tendency of bilateral eye involvement which stresses the importance of immediate action what concerns therapy of these patients

In the following some of the cases will be briefly mentioned and commented

Case no 4 is an example of monolateral eye involvement in a man aged 57 He was admitted with a visual acuity of finger counting (f c) 2 m on the right (d) eye which yielded a decrease in corneal pulse amplitudes to 46 per cent of the normal mate eye values as shown in Fig 1 The amplitudes of the mate eye was normally sized which indicated that there was no imminent danger of involvement of this normal mate eye One year later his left subclavian artery was partially occluded possibly because of a giant cell arteritis lesion at this site

Case no 1 (male aged 71) was admitted in January 1967 with bilateral symptoms and a visual acuity of 1 m f c in right eye and amaurosis in the left With a provisory set up the corneal pulse amplitudes were measured to equal 2 μ in both eyes One year later the amplitudes were normal in magnitude and the vision was 6 m f c in right eye and amaurosis in left eye This demonstrates the fact that following adequate therapy the occluded artery may re canalize with increase in blood supply and what is important with increase in vision in the eye which initially yielded a visual acuity of finger counting If, however the eye is amaurotic or yields only light perception when treatment is started we have never experienced any increase in function although the corneal pulse amplitudes may rise to sub normal or normal levels

Case no 2 (male aged 76) had suffered from diplopia of one week duration when he suddenly became amaurotic on the right eye. Initially

he suffered no symptoms from the left eye which yielded a visual acuity of 5/10, although the dynamic tonometry test demonstrated a bilateral involvement of ocular blood supply (see Table 1) One month later following treatment and still on steroids he got an attack of leftsided amaurosis fugax of 5 minutes duration Four months later, still on steroids and with a normal SR of 11 mm per hour he wakened from his afternoon nap amaurotic on both eyes The vision on left eye was completely gone for 2 hours but returned afterwards to 5/7 5 In comment to this observation the blindness in Case no 10 (female, aged 77) was also first noticed on waking

Case no 3 (male, aged 66) suffered from symptoms in the left eye of four days duration when he was admitted in our department in March 1968 His left fundus demonstrated ischemic changes with exception of the part nourished from a cilioretinal artery, his right fundus was normal The visual acuity was 5/10 on the right side, 1 m f c on the left The corneal pulse amplitude measured 20 μ in the right eye, which is in the lower normal range and made us suspect a slight involvement also in the right ophthalmic artery in spite of the normal fundus picture On the left side the amplitudes were 12 μ which is a definite decrease, as shown in Fig 2 Steroids had good effect on the SR, the corneal pulse amplitudes continued, however, to decrease on the left side Our suspicion concerning right eye involvement turned out to be valid, the sixth day his vision on right eye fell to 5/50 and ischemic lesions were demonstrated in his right eye fundus Treatment was increased including Rheomakrodex infusions and two months later his vision was 5/10 in both eyes The follow up period was complicated with several attacks of broncho pneumonia Half a year later he suddenly got a new attack of his giant cell arteritis, with zero corneal pulse amplitudes and reduction of visual acuity to 5/15 — in both eyes The treatment was once again increased and vision improved to 5/10 on right side and 5/7 5 on the left side where his cilioretinal artery

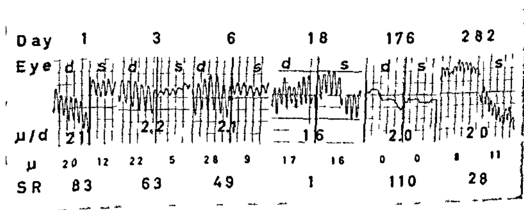


Fig 2

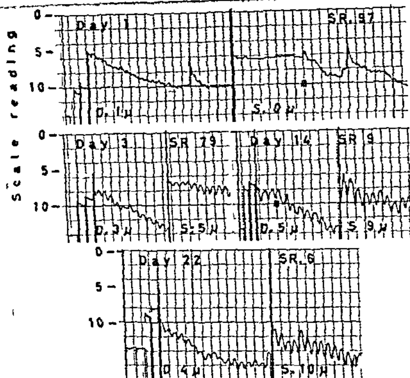


Fig 3

was still functioning At the latest control on day 452 the corneal pulse amplitudes measured 15 and 16 μ in the respective right and left eye

Case no 7 (male aged 76) yielded I p on right eye with no symptoms from his left eye which demonstrated a visual acuity of 5/7 5 The dynamic tonometry test results are presented in Fig 3 a bilateral involvement of ocular blood supply was found The following day an ischemic lesion at the disc margin was noted in the left eye treatment yielded excellent results with no reduction in vision of this left eye

Case no 8 (female aged 68) yielded I p on left (s) eye with no symptoms from the mate eye at admittance in our department The dynamic tonometry test yielded however, decreased corneal pulse amplitudes in both eyes demonstrating a bilateral involvement as shown in Fig 4 The corneal pulse amplitudes increased on both sides following treatment, which indicates that this test may offer valuable information also concerning the effect of treatment

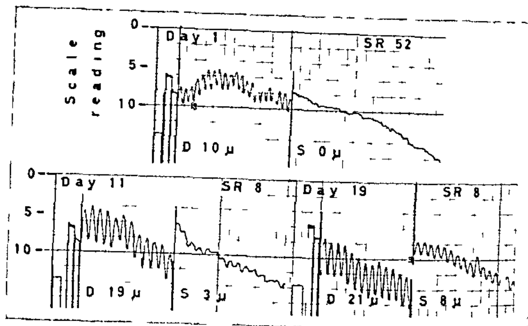


Fig 4

Comment

The ocular blood flow consists of two parameters, the non pulsatile flow which is equal in size through the total heart cycle, and the pulsatile flow which enteres the eye in systole The excess of blood which enters the eye in systole because of this pulsatile flow initiates a pulsesynchronous change in intraocular pressure which may be recorded by use of dynamic tonometry If a decrease in ocular blood supply exists, as in internal carotid artery occlusion, a corresponding decrease may be noted in the corneal indentation pulse amplitudes (*Castren & Laulkainen 1964, Bynke 1966, Bron et al 1967, Galin 1967*) A decrease in intraocular pulsation have also been demonstrated in luetic choroidal atrophy (*Suzuki 1962*) and in our department by tapetoretinal degenerations In central retinal artery embolism only a minor, 10 per cent decrease exists in the intraocular pulsation (*Thiel 1928, Suzuki 1962*), probably because of normal choroidal blood supply of these eyes This important fact was also confirmed by dynamic tonometry test results obtained in 4 fresh and typical cases of central retinal artery embolism in our department Accordingly, this test may be helpful in order to differentiate between central retinal artery embolism and giant cell arteritis, two diseases which may yield identical ophthalmoscopical findings

In the present study a marked decrease in corneal pulse amplitudes was demonstrated in eyes suffering from giant cell arteritis, which strongly suggests that a corresponding decrease exists in both retinal and choroidal blood supply in these cases The zero pulse amplitude recorded

in Case no 7 in the one eye with a visual acuity of 5/7 5 indicates that the pulsatile flow may be stopped completely while the eye still receives sufficient nourishment from the remaining non pulsatile flow

Meadows (1968) stresses the point that the onset of blindness in giant cell arteritis is usually abrupt and often first noticed on waking, an observation which is confirmed by Case no 2 and Case no 10 in the present study *McGowan (1967)* reports a case of giant cell arteritis which was amaurotic in one eye and developed amaurosis in the other eye following general anesthesia A similar case was recently observed in Oslo City Hospital (*Bergaust 1968*) in this case the diagnosis of giant cell arteritis was verified after general anesthesia was given with amaurosis as a result Most probably these eyes which yielded no symptoms prior to general anesthesia still had a reduced ocular blood supply as a consequence of giant cell arteritis lesions in their ophthalmic arteries This possibility has been proved valid in some of the cases presented in the present study The above observations may be explained by the fact that a marked decrease in corneal pulse amplitudes is also initiated by sleep following Seconal (meballymal) or Thiopentone (thiomebumal) administration and during ether or Halothane general anesthesia (*Hørven & Syrdalen 1970*) When this anesthesia effect comes in addition to the reduction in ocular blood supply induced by the giant cell arteritis, a further decrease in corneal pulse amplitudes and ocular blood supply may be initiated with amaurosis as a result As a consequence of this interpretation it is advisable for patients suffering from giant cell arteritis to have a dynamic tonometry test performed prior to accepting surgery under general anesthesia If this test demonstrates a decrease in corneal pulse amplitudes in eyes with useful vision, the general anesthesia should if possible be postponed

Summary

Dynamic tonometry have been performed in 10 patients suffering from giant cell arteritis Seven of the patients complained of *symptoms in one* eye and three in both eyes at admittance in our department The dynamic tonometry test demonstrated however, a bilateral involvement of the ocular blood supply in 8 of the patients Thus dynamic tonometry is regarded as a sensitive accurate and safe clinical test which offers results of diagnostic and prognostic importance in these patients Moreover, the test offers a unique opportunity to differentiate patients suffering from giant cell arteritis from central retinal artery embolism as the latter group of patients yield normal or close to normal corneal pulse amplitude values even when the eye is amaurotic

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From Oslo University Eye Department Rikshospitalet Oslo Norway
(Head Professor dr med. Thore L. Thomassen)

CORNEAL INDENTATION PULSE AND RETROBULBAR ANESTHESIA

By

Per Syrdalen and Ivar Hørven

During general anesthesia a striking decrease in corneal indentation pulse amplitudes have been demonstrated by use of dynamic tonometry (*Hørven & Syrdalen 1970*) This decrease in amplitudes is probably reflecting a corresponding decrease in ocular blood supply, which may explain why general anesthesia may initiate disastrous results in patients suffering from giant cell arteritis (*McGowan 1967*)

The present investigation was performed in order to study if a similar change in corneal indentation pulse amplitudes might be initiated by retrobulbar anesthesia If so, the study should offer information whether the decrease in amplitude was caused by the anestheticum itself the adrenalin (Exadrin) or the vehicle injected

Material

The material consists of 67 patients with the following disorders Various forms of glaucoma 32 retinal detachment 21 choroidal melanoma 12 strabismus 2 There were 23 males and 44 females and the age averaged 61 8 years (24–83)

The material was divided at random in the following groups based upon the drug injected

A Xylocain Exadrin 1%† 20 patients 3 males and 17 females Average age 63 9 years (29–83) (Retinal detachment 10 glaucoma 7 strabismus 2 choroidal melanoma 1)

B Xylocain Exadrin 2%† 20 patients 7 males and 13 females Average age 58 7 years (24–81) (Choroidal melanoma 7 retinal detachment 7 glaucoma 6)

† Xylocain Exadrin 1 resp 2 contains lidocain chloride 10 mg resp 20 mg and adrenalin 0 01 mg resp 0 0125 mg per ml Exadrin contains adrenalin 0 0125 mg per ml and was kindly supported by A/B Astra Sweden

C Xylocain 1% 20 patients, 9 males and 11 females Average age 63 1 years (35–77) (Glaucoma 15, retinal detachment 4, choroidal melanoma 1)
D Xylocain 2% 1 female patient aged 45 (Glaucoma)
E Exadrin† 3 males with an average age of 75 (70–80) (Glaucoma absolutum 3)
F Saline 0 9% 3 patients, 1 male and 2 females Average age 52 3 years (44–60) (Choroidal melanoma 3)

Only groups A, B and C consist of a fair number of patients, they are not, however, directly comparable as Group C is over represented with glaucoma patients

Group D consists of only one patient The second patient we gave Xylocain 2% developed a severe side reaction with loss of consciousness and fall in arterial blood pressure The cause of this side reaction was probably leakage of the anestheticum into the optic nerve sheats and into the cranial cavity This reaction subsided completely in a couple of hours without leaving any traces Due to this side reaction we did not use Xylocain 2% without adrenalin to other patients

The three patients in Group E which initially received Exadrin were afterwards given Xylocain 2% with a percentage reduction in corneal indentation pulse amplitude of a similar order of magnitude as seen in the patient of Group D (see also Table II)

A retrobulbar injection of Exadrin or Saline followed by a second injection of anestheticum was restricted to patients with eyes which were to be removed A limitation of available cases existed which explains why Group E and Group F only consist of three patients each By chance Group E happened to consist of hypertensive glaucomatous eyes and Group F of hypotensive choroidal melanoma eyes (Dunnington 1938, Horven 1969)

Methods

On the day of surgery dynamic tonometry (Horven 1968) was performed under topical anesthesia (oxibuprocain) Immediately afterwards a retrobulbar injection of 4 5 ml was given, as specified for the various groups listed above A second dynamic tonometry was performed 10 minutes after the retrobulbar injection

The eye tension was measured in scale reading Schiotz and converted into mm Hg intraocular pressure (P_0) by use of Friedenwald's 1955 converting table In Group A the eye tension was measured with the 5 5 and 10 g plunger weight in order to evaluate the scleral rigidity by use of Friedenwald's 1955 nomogram

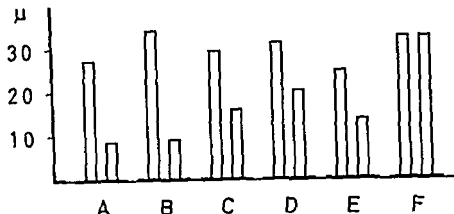


Fig 1
Average corneal indentation pulse amplitude in μ before and after retrobulbar injection in the various groups of patients

The corneal indentation pulse amplitudes were recorded in microns of plunger movement (μ) and converted into mm³ change in ocular volume (ΔV) by use of the converting table based on Langham-Hetland-Eriksen s data as previously described (Horven 1970a)

Visual acuity was recorded before and 8 minutes after injection in all cases of Group C

The statistical method of paired comparison was applied to the data obtained before and after injection within the groups When the various groups were compared with each other, the Student s t test was applied The statistical significance levels are indicated as follows *=significant at the 5% level **=significant at the 1% level ***=significant at the 0 1% level

Results

The results obtained are specified as to change in corneal indentation pulse amplitudes (μ) ocular volume (ΔV) and intraocular pressure (mm Hg) as shown in Table I Figure 1 visualizes the change in μ obtained in the various groups of patients

Saline No significant change in μ ΔV or mm Hg was obtained in Group F Most probably therefore, the vehicle itself is not responsible for the changes presented below A typical recording is shown in Figure 2

Exadrin A significant (*) decrease in μ and ΔV was obtained following retrobulbar injection of Exadrin (Group E) with an average reduction to 54% and 52 2% respectively, of the value obtained before injection A minor and not significant decrease to 87% was observed in mm Hg intraocular pressure (Table I)

C Xylocain 1% 20 patients, 9 males and 11 females Average age 63 1 years (35–77) (Glaucoma 15, retinal detachment 4, choroidal melanoma 1)

D Xylocain 2% 1 female patient aged 45 (Glaucoma)

E Exadrin† 3 males with an average age of 75 (70–80) (Glaucoma absolutum 3)

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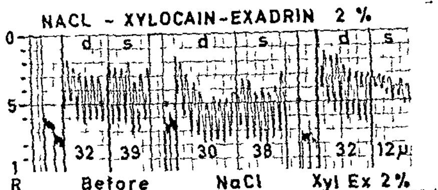


Fig 2

No decrease in corneal indentation pulse amplitudes following left side retrobulbar injection of saline Decrease of corneal indentation pulse amplitudes following injection of Xylocain Exadrin d=right eye s=left eye

Xylocain The anestheticum was injected in two concentrations 1% (Group C) and 2% (Group D and Group E) In Group E the patients had on beforehand received a retrobulbar injection of Exadrin as previously described The results from this Group E is given in Table II An average reduction in μ to 53 3% (Group C) 64 5% (Group D) and 57 5 % (Group E) was obtained Typical recordings from Group C and Group D are presented in Figure 3 and Figure 4

Table II

Results obtained by retrobulbar injection of Exadrin followed by Xylocain 2%

	Exadrin		Xylocain 2%	
	Before	*After*	*Before*	*After*
μ (average)	24 67	13 33	13.33	7 67
σ (of pop)	10 26	7 09	7 09	3 21
% $\left(\frac{\text{After } 100}{\text{Before}}\right)$	54 0		57 5	
t value/ sign level	6 107*		2 125	

The results indicate that there *is no difference in* corneal indentation pulse amplitude reducing effect by 1% or 2% Xylocain both concen*trations yielding* a reduction in μ to about 50–60% of the value obtained before injection This indication is offered with the reservation that the groups are not directly comparable only Group C consists of a fair number of patients In this *Group C* (Xylocain 1%) there was a highly

Table I

Dynamic tonometry results (average) in the various groups of patients The statistical method of paired comparison is applied to the results obtained before and after retrobulbar injection

Significance levels *=5% **=1%, *** = 0 1%

	Group A Xyl Exadr 1%		Group B Xyl Exadr 2%		Group C Xyl 1%		Group D Xyl 2%		Group E Exadrin		Group F Saline	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
N	20	20	20	20	20	20	1	1	3	3	3	3
μ (average)	27 15	8 40	33 95	8 90	29 35	15 65	31 00	20 00	24 67	13 33	32 33	32 33
σ (of pop)	13 11	7 26	11 46	4 69	10 14	8 66			10 26	7 09	9 07	8 14
% $\left(\frac{\text{After } 100}{\text{Before}}\right)$	30 9		26 2		53 3		64 5		54 0		100	
t value/sign level	10 669***		10 857***		10 559***				6 107*			
ΔV (average)	2 84	0 87	3 41	0 91	3 26	1 68	3 50	2 60	2 95	1 54	3 17	3 13
σ (of pop)	1 86	0 88	1 33	0 47	1 30	1 23			1 31	0 82	0 94	0 82
% $\left(\frac{\text{After } 100}{\text{Before}}\right)$	30 8		26 7		51 6		74 3		52 2		98 7	
t value/sign level	7 937***		10 264***		7 668***				4 978*		0 115	
I_0 (average)	14 95	13 08	17 33	13 56	29 11	21 41	24 40	31 60	76 60	66 67	8 43	9 50
σ (of pop)	7 29	6 42	12 58	11 00	19 24	13 41			22 07	13 11	4 79	4 29
% $\left(\frac{\text{After } 100}{\text{Before}}\right)$	87 5		78 2		73 5		129 [illegible]		87 0		112 7	
t value/sign level	2 747*		2 700*		2 692*				1 75[illegible]		1 031	

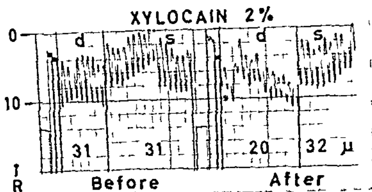


Fig 4
Decrease in corneal indentation pulse amplitudes following right side retrobulbar injection of Xylocain 2%

significant (***) decrease both in μ and ΔV with an average reduction to 53 3% and 51 6%, respectively, of the value obtained before injection A significant (*) decrease to 73 5% was also noted in mm Hg intraocular pressure However, Group C contained a fairly high number of glaucoma patients with increased intraocular pressure, which explains the high average mm Hg intraocular pressure values presented in Table I

Xylocain Exadrin Concentrations of 1% (Group A) and 2% (Group B) were tested Following retrobulbar injection a highly significant (***) reduction in μ and ΔV was demonstrated to average 26–31% of the value obtained before injection (Table I) A significant (*) decrease was also noted in the mm Hg intraocular pressure to average 87 5% (Group A) and 78 2% (Group B) of the value obtained before injection A typical recording is presented in Figure 5

No significant difference was found in μ, ΔV or mm Hg intraocular pressure between Group A and Group B as judged by the results obtained by application of the Student s t test which are summarized in Table III This strongly indicates that a maximal corneal indentation pulse amplitude reducing effect is obtained with the 1% solution no further reduction is to be expected by increasing the concentration to 2% The fact that Xylocain Exadrin 1% contains 0 01 mg adrenalin per ml while Xylocain Exadrin 2% contains 0 0125 mg adrenalin per ml may probably explain the minor but not significant difference which exists between these two groups (Table I)

As seen in Table III there is a significant (**) difference in corneal indentation pulse amplitude reduction between Group A and C and between Group B and C as judged by the results obtained by application of the Student s t test The decrease in amplitude is more pronounced in the two groups which received Xylocain Exadrin

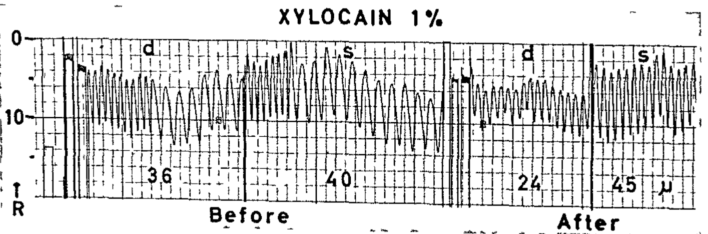


Fig 3

Decrease in corneal indentation pulse amplitudes following right side retrobulbar injection of Xylocain 1%

Table IV

Visual acuity before and 8 minutes after retrobulbar injection of Xylocain 1%
(Group C N=20)

	5/5–5/15	5/20–5/50	c.f	l.p	nil
Before	13	5	2		
After	2	10	3	2	3

obtained before injection compared with 0 0189 after injection, with a t value of 1 502, as judged by the statistical method of paired comparison

Discussion

A striking decrease of similar order of magnitude have been initiated in corneal indentation pulse amplitudes by retrobulbar injection of either Exadrin or Xylocain Evidence is offered suggesting that the two drugs act through different trigger mechanisms in their corneal indentation pulse amplitude reducing capacity, as a combined effect is obtained when the two drugs are injected simultaneously In order to evaluate the mechanisms behind this effect, some possibilities may be excluded

First the injected volume of fluid may be ruled out as a possible cause to the decrease in amplitude, as there was no change in amplitudes in Group F which received saline Second, a general effect of the drugs is not responsible for the decrease in amplitudes because the corneal indentation pulse amplitudes as a rule were unchanged in the control mate eye as shown in Figures 1, 2 3 4 Third it is known that a very low scleral rigidity may produce small corneal indentation pulse amplitudes (Syrdalen 1970) No significant change in scleral rigidity was, however noted in our patients

Fourth, it has previously been shown that the corneal indentation pulse amplitudes may change with the intraocular pressure levels (Horven 1970b) If the intraocular pressure (P_t) is higher than the systolic pressure in the ophthalmic artery, no blood will enter the eye and a zero amplitude will be recorded As the intraocular pressure drops the amplitudes will increase in size until a maximum is reached at a P_t value of 40–50 mm Hg With a further drop in P_t the amplitudes will decrease, this decrease is however rather limited in the normal range of intraocular pressure As the present material contains eyes at various intraocular pressure levels the slight decrease in intraocular pressure which in most cases was induced by the retrobulbar injection may have implied a minor change in corneal indentation pulse amplitudes *This change may be an* increase or decrease in amplitudes dependent on the intraocular pressure levels before and after injection in the various eyes No attempt has been

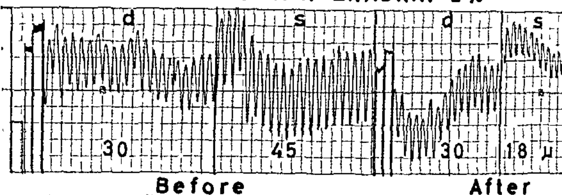


Fig 5
Decrease in corneal indentation pulse amplitudes following left side retrobulbar injection of Xylocain Exadrin 2%

To summarize, the results demonstrate that a retrobulbar injection of Exadrin yields an average amplitude reduction to about 54% of the original values A retrobulbar injection of Xylocain 1% or 2% yields a similar decrease in amplitude to about 50–60% of the value obtained before injection However, if the Xylocain is injected after the Exadrin, or if the two drugs are injected simultaneously, a reduction in amplitudes to about 26–31% of the original values is obtained It may therefore be concluded that Exadrin and Xylocain most probably act through different trigger mechanisms in their corneal indentation pulse amplitude decreasing capacity the full effect of one of the drugs does not block the effect of the other drug

Visual acuity Visual acuity was performed before and 8 minutes after injection of Xylocain 1% in Group C, a temporary decrease was found in 19 of the 20 patients and is listed in Table IV All patients regained their original visual acuity when the effect of the anestheticum was subsided

Scleral rigidity calculations demonstrated no significant change before and 10 minutes after retrobulbar injection of Xylocain Exadrin 1% in the 20 patients of Group A An average scleral rigidity value of 0 0207 was

Table III
Comparison between Group A B and C before and after retrobulbar injection
The table offers t values obtained by use of Student s t test

	µ		ΔV		mm Hg	
	Before	After	Before	After	Before	After
Group A/Group B	1 746	0 259	1 105	0 168	0 732	0 169
Group A/Group C	0 594	2 848**	0 821	2 389*	3 078**	2 507*
Group B/Group C	1 344	3 045**	1 116	2 786**	2 293*	2 025*

Table IV

Visual acuity before and 8 minutes after retrobulbar injection of Xylocain 1%
(Group C N = 20)

	5/5–5/15	5/20–5/50	c.f	l p	nil
Before	13	5	2		
After	2	10	3	2	3

obtained before injection compared with 0 0189 after injection, with a t value of 1 502, as judged by the statistical method of paired comparison

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A striking decrease of similar order of magnitude have been initiated in corneal indentation pulse amplitudes by retrobulbar injection of either Exadrin or Xylocain Evidence is offered suggesting that the two drugs act through different trigger mechanisms in their corneal indentation pulse amplitude reducing capacity, as a combined effect is obtained when the two drugs are injected simultaneously In order to evaluate the mechanisms behind this effect, some possibilities may be excluded

First the injected volume of fluid may be ruled out as a possible cause to the decrease in amplitude, as there was no change in amplitudes in Group F which received saline Second, a general effect of the drugs is not responsible for the decrease in amplitudes, because the corneal indentation pulse amplitudes as a rule were unchanged in the control mate eye as shown in Figures 1 2 3, 4 Third it is known that a very low scleral rigidity may produce small corneal indentation pulse amplitudes (Syrdalen 1970) No significant change in scleral rigidity was, however, noted in our patients

Fourth it has previously been shown that the corneal indentation pulse amplitudes may change with the intraocular pressure levels (Horven 1970b) If the intraocular pressure (P_t) is higher than the systolic pressure in the ophthalmic artery no blood will enter the eye and a zero amplitude will be recorded As the intraocular pressure drops the amplitudes will increase in size until a maximum is reached at a P_t value of 40–50 mm Hg With a further drop in P_t the amplitudes will decrease this decrease is however rather limited in the normal range of intraocular pressure As the present material contains eyes at various intraocular pressure levels the slight decrease in intraocular pressure which in most cases was induced by the retrobulbar injection may have implied a minor change in corneal indentation pulse amplitudes This change may be an increase or decrease in amplitudes dependent on the intraocular pressure levels before and after injection in the various eyes No attempt has been

made to evaluate the total effect on the amplitude sizes in our material which may be caused by the minor decrease in intraocular pressure following injection, as no proper method is available at present for such an evaluation It is obvious, however, that the slight decrease in average intraocular pressure can explain only a minor and probably negligible part of the marked decrease in amplitudes following retrobulbar injection in our material

It may be assumed that the corneal indentation pulse amplitudes primarily reflects the pulse synchronous change in ocular volume initiated by the excess of blood entering the eye in systole Theoretically, if the blood flow was non pulsatile, i e, if the same volume of blood entered the eye per time unit in diastole and systole, no pulsations would exist in the intra ocular pressure and zero amplitudes would be recorded by dynamic tonometry, even if the total ocular blood flow was unchanged It is quite possible that the decrease in corneal indentation pulse amplitudes observed following retrobulbar injection of xylocain may be caused by a change from pulsatile towards non-pulsatile blood flow, as xylocain possesses a vasodilatatory effect (Dhuner & Lewis 1966, Goldman *et al* 1966)

On the other hand, if a decrease exists in the total ocular blood supply, this decrease would be reflected also in the pulsatile part with a corresponding decrease in corneal indentation pulse amplitudes As known, Exadrin (adrenaline) stimulates both α (constrictor) and β (dilator) receptors By the dose applied in the present study Exadrin most probably will induce vasoconstriction (de la Lande & Whelan 1959) with a corresponding reduction in ocular blood supply If this view is valid the reduction to 54% in corneal indentation pulse amplitudes following retrobulbar injection of Exadrin is initiated by a corresponding decrease in ocular blood supply Following intramuscular injection, Dhuner & Lewis (1966) found that the vasoconstrictor action of epinephrine did no more than offset the vasodilator action of Xylocain, the resultant blood flow was therefore not statistically significantly different from the saline control It is stressed that the corneal indentation pulse amplitudes recorded by dynamic tonometry primarily reflects a pulse synchronous change of intraocular volume and offers no direct information upon ocular blood flow The marked decrease of corneal indentation pulse amplitudes observed following retrobulbar injection of Xylocain Exadrin offers, therefore, no conclusive evidence upon the ocular blood flow through these eyes

The reduction in intraocular pressure seen in our Group A, B and C is only confirming the observation known for long that retrobulbar anesthesia is producing a certain degree of hypotonia The cause of this

reduction has been explained from reduced inflow of aqueous humor (de Roetth & Carroll 1955) The reduced inflow of aqueous humor is partly produced by vasoconstriction caused by adrenaline (Duke Elder 1962) The hypotonia may also be caused by the anestheticum itself by blocking the parasympathetic activity of the third nerve and the ciliary ganglion (Gifford 1949) Atkinson (1961) explained lowered intraocular pressure as a result of decrease of blood within the choroid due to constriction of the arteries entering the globe

Carroll and de Roetth (1955) demonstrated a similar effect on visual acuity after retrobulbar anesthesia with procaine as observed in our Group C This effect is explained by absorption of the anestheticum into the optic nerve

Summary

A significant reduction in corneal indentation pulse amplitudes as recorded by dynamic tonometry is demonstrated following retrobulbar injection of either Xylocain, Exadrin or Xylocain Exadrin Evidence is offered suggesting that Exadrin and Xylocain act through different trigger mechanisms in their amplitude decreasing capacity the full effect of one of the drugs does not block the effect of the other drug

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From The Departments of Neurosurgery and Ophthalmology Aarhus Kommune hospital and Odense Amts og Bys Sygehus Denmark

CAROTID CAVERNOUS FISTULAE

A Study of 18 Cases

By

P H Madsen

Pulsating exophthalmos is usually due to an abnormal communication between the internal carotid artery and the cavernous sinus In most cases the condition develops after severe head injuries especially in the presence of fracture of the base of the skull, by which the internal carotid is injured in its course through the cavernous sinus The relation between the artery and the surrounding sinus is so intimate that a lesion of the artery invariably results in entry of blood into the sinus, from which it is forced into the veins usually those entering the orbit However, in from one quarter to one third of the patients the fistula occurs spontaneously (Hamby 1966 Stern Brown and Alksne 1967, Sanders and Hoyt 1969) Traumatic fistulae are most frequently encountered in men whereas there is a female preponderance in the spontaneous group It is likely that some of the spontaneous fistulae develop on rupture of an aneurysm in the intracavernous portion of the internal carotid artery Jefferson (1938) even expressed the view that this was the causal mechanism in most carotid cavernous fistulae Spontaneous fistulae occasionally develop during the latter part of pregnancy or during labour and arteriosclerosis seems to be a contributory cause in other cases

Most commonly the disease is unilateral, but it may be bilateral if there is a wide communication between the cavernous sinuses on the right and left sides Such inter cavernous communications are of normal occurrence but they are usually very narrow (Dandy 1937 Hamby 1966) In a few cases the fistula is followed by contralateral exophthalmos (David *et al* 1964 Graham 1966 Bynke 1969)

The manifestations are of fairly rapid onset occurring shortly after the trauma Figure 1 shows a typical example of carotid cavernous fistula in a 22 year-old man Very characteristic are the unilateral exophthalmos with pulsation of the eye and in step with the heart beats a pulse synchronous loud bruit in the same side of the head and above the orbit

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important to ensure that there is blood supply to both halves of the brain Conditions which require differentiation are orbital encephalocele, vascular orbital tumour tumour of the optic nerve and meningeoma of the olfactory nerves, which produce symptoms which are reminiscent of those of carotid cavernous fistula (Walsh 1957, Higazi and El Banhawy 1964, Hamby 1966) I have observed distinctly pulsating exophthalmos in two patients in whom the orbital roof has been removed after traumatic injury, but angiography did not reveal a fistula in these patients



Fig 2
Right common carotid angiogram showing carotid-cavernous fistula draining to orbital veins in a 65 year-old man (Case 6) (Subtractionangiogram)

The disease is treated by producing thrombosis in the arteriovenous communication

1 *Spontaneous thrombosis* may be seen in rare cases (Knudtzon 1950) Dandy (1937) reported that spontaneous healing occurred in 10%, but *this figure is too high* In his analysis, he included patients who had been

The marked hyperaemia of the cavernous sinus and the orbital veins is transmitted to the vessels on the forehead and in the conjunctiva, resulting in large, tortuous, dilated veins and lid oedema



Fig 1
Left sided carotid cavernous fistula in a 22 year old man (Case 8)

In relation to the pulsating exophthalmos, disturbances of the ocular movements often occur Paresis involves the abducent nerve more frequently than the oculomotor and trochlear nerves However, in many cases, the limitation of ocular movements is of a mechanical nature, due to orbital oedema Vision is frequently impaired, and atrophy of the optic nerve may occur Ophthalmoscopic examination reveals marked venous congestion and, sometimes, mild papilloedema and extravasation of blood Secondary glaucoma may also be observed in rare cases (Henderson and Schneider 1959, Sanders and Hovt 1969)

Even though the fistula may produce greatly discomforting symptoms, it is an immediate advantage for the patient that the arterial blood, instead of entering the cranial cavity, passes direct into the veins However, this involves the risk of vascular insufficiency in the region of the brain which is supplied by the upper portion of the internal carotid, with ensuing cerebral manifestations Another complication is venous congestion in the nasal cavity, which may lead to fatal epistaxis

The diagnosis is made on the basis of the typical clinical picture and carotid angiography (Fig 2) By angiography on the contralateral side it

is important to ensure that there is blood supply to both halves of the brain Conditions which require differentiation are orbital encephalocele, vascular orbital tumour, tumour of the optic nerve and meningeoma of the olfactory nerves, which produce symptoms which are reminiscent of those of carotid cavernous fistula (Walsh 1957, Higazi and El Banhawy 1964, Hamby 1966) I have observed distinctly pulsating exophthalmos in two patients in whom the orbital roof has been removed after traumatic injury, but angiography did not reveal a fistula in these patients



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subjected to operation, but in whom healing occurred later than three weeks postoperatively

2 *Prolonged compression of the internal carotid in the neck* was previously a commonly used method (Hamby 1966, Isfort 1967) It was recommended by Dandy in cases in which it was desired to avoid even a small operation

3 *Ligation of the common and, possibly, the external carotid*

4 *Ligation of the internal carotid in the neck*

Until a few years ago, procedures 3 and 4 were the most commonly used therapeutic measures

5 Ligation of the internal carotid in the neck and intracranially above the fistula (*trapping operation*) In this operation, an attempt is made to place the ligature caudalward to the ophthalmic artery, but sometimes it is also necessary to ligate the latter

6 Ligation of the internal carotid in the neck and, perhaps, also intracranially, supplemented by *muscle embolisation of the fistula* (Brooks 1931, Hamby 1964, 1966) A silver clipped muscle strip is introduced into the internal carotid and forced up to the fistula, which is then closed

7 *Embolisation by other agents*, such as gelfoam or radio opaque measured beads

8 *Direct intervention* on the cavernous sinus or excision of orbital veins

Clinical Material

The series studied consisted of 18 patients with carotid cavernous fistula, 12 from Aarhus Kommunehospital and six from Odense Amts og Bys Sygehus In 17 cases, the fistula was confirmed by carotid angiography, while this method of examination was not used in the last patient, a 72 year-old woman, who was not subjected to operation

Clinical data concerning the 18 patients are listed in Table 1 (before treatment) and Table 2 (after treatment) There were 13 men and five women In two of the women, the fistula occurred spontaneously without any demonstrable preceding trauma, while, in the remaining cases, the carotid cavernous fistulae were referable to severe head injuries, in 10 of the patients, fracture of the base of the skull was present

Carotid cavernous fistulae may be encountered in all age groups The fistula was situated on the right side in 11 cases and on the left side in six, while bilateral fistulae were seen in one Fourteen patients had unilateral ocular symptoms on the ipsilateral side, while three had a unilateral fistula with bilateral ocular symptoms (Cases 2, 10 and 12)

Spontaneous fistula occurred in two women aged 63 and 49 years In the first of these patients, carotid angiography revealed a hazelnut sized saccular aneurysm on the internal carotid at the cavernous sinus (Fig s 3 and 4) Marked exophthalmos, lid oedema, abolition of ocular move-



Fig 3
Right common carotid angiogram with saccular aneurysm (arrow) in the cavernous sinus and drainage to a very dilated orbital vein in a 63 year-old woman with spontaneous carotid cavernous fistula (Case 1)

ments and corneal anaesthesia were present, and there was absolute glaucoma of the eye (Fig 5) After ligation of the common carotid artery the exophthalmos and the orbital and lid oedema resolved but ophthalmoplegia and corneal anaesthesia persisted and the eye remained blind (Fig 6) In the second patient no carotid aneurysms were demonstrated

In the remaining 16 patients the fistulae were of *traumatic origin* The nature of the traumata sustained appears from Table 1 The symptoms of the arteriovenous fistula developed from a few days to weeks after the accident Table 1 also shows the time when exophthalmos was first observed In most cases paresis of the ocular muscles and a bruit synchronous with the pulse developed within a few days while exophthalmos and lid oedema occurred later

One of the patients a 26 year old man (Case 15) suffered from mild arterial hypertension and the five oldest patients in the series (Cases 6 12 13 17 and 18) revealed radiographic signs of aortic and carotid arteriosclerosis

Lid oedema and dilated tortuous vessels in the conjunctiva and orbital region were observed in all patients (Fig 7) With just one exception (Case 1) a *pulse synchronous bruit* — observed by the patients and recognised by auscultation — was present in all cases causing great discomfort



Fig 4
Anteroposterior view of the same patient (Arrow indicates the aneurysm)

to the patients *Exophthalmos* was also present in all except one (Case 14) This patient had dilated, pulsating vessels in the eyelid and conjunctiva and oedema of the orbital region In most of the patients, the exophthalmos was fairly distinct, measuring 5–10 mm as compared with the other eye Two patients had exophthalmos, but no pulsation (Cases 1 and 15) The pulsation was occasionally very slight For example, in Case 2 it could be recognised only under the slit lamp The remaining patients had distinct pulsation of the eyeball and the vessels in the medial canthus

The ocular manifestations were unilateral in 14 patients One patient had bilateral fistulae and bilateral exophthalmos In three cases, the fistula was unilateral, but was accompanied by bilateral ocular signs Strikingly enough, in these patients (Cases 2, 10 and 12) the pulsating exophthalmos and the palpebral and conjunctival oedema were most pronounced on the contralateral side In Case 10, even post traumatic



Fig 5
Right sided spontaneous carotid cavernous fistula in a 63 year-old woman (Case 1)

enophthalmos developed on the affected side to be followed later by proptosis of the eye

Visual acuity in the patients before the treatment is listed in Table 1 It is seen that it ranged from 0 5 to 1 0 in 12 eyes in 11 patients, and one had a vision of 0 25 In three patients it was impossible to determine the visual acuity Three patients had no light perception in the five affected eyes, one of these had absolute glaucoma and another was blind because of a direct trauma to the eye All patients with unilateral symptoms revealed a visual acuity ranging from 0 67 to 1 0 in the unaffected eye



Fig 6
The same patient five months after ligation of the common carotid artery (Case 1)



Fig 4
Anteroposterior view of the same patient (Arrow indicates the aneurysm)

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								RI Lnoq l tl —	+	+	No LI	No ı ove c ts	Nor ı al
								exoq l tl					V treous l aen
10	M	22	R	Traun at	Exp los o ı	?		LI +	+	+	No I I	No movements after eye les oı	
11	M	45	R	Traun at c	On bicycle hit by car	3		+	+	+	Unconscious	No movements	Normal
12	M	65	L	Traumatic	Moped accident	23		RI +	+	+	No LP	No movements	Normal
								LE +	(+)	+	No LP	No movements	Normal
													Venous stasis
13	F	72	L	Traumatic	Walking hit by car	6		+	+	+	0 5	No movements	blurred disc
14	M	17	R	Traumatic	Fall 6 metres	30	dilated veins	—	+	+	?	Impaired movements	Normal
15	M	26	R	Traumatic	Scooter accident	12		+ (no pulsation)	+	+	0 67	Slight III + VI paresis	Venous stasis
16	M	42	R	Traumatic	Head squeezed between 2 rollers in a papermill	23		+	+	+	0 5	VI paresis	Venous stasis
17	F	53	R	Traumatic	On moped hit by car	20		+	+	+	1 0	VI paresis	Slight venous stasis
18	M	70	Bilateral	Traumatic	On bicycle hit by car	2		RE (+)	+	+		Divergent eyes	
								LE (+)	+	+	Unconscious	no movements	?

Table I

Data concerning the 18 patients with carotid cavernous fistula

Case	Sex	Age, in years	Side involved	Type	Trauma	Exophthalmos after trauma No of days	Exophthalmos	Chemosis dilated veins	Bruit	Visual acuity	Motility of the eye	Ophthalmoscopy
1	F	63	R	Spontaneous			+ (no pulsation)	+	−	No LP	No movements	Extensive haemorrhage
2	F	49	R	Spontaneous			RE +	(+)	+	1 0	VI paresis	Slight venous stasis
3	M	17	L	Traumatic	Fall 3 metres	14	LE +	+	+	0 67		”
4	F	16	R	Traumatic	On bicycle hit by car	12	+	+	+	0 67	VI paresis	Normal
5	M	29	L	Traumatic	Motor cycle accident	6	+	+	+	0 67	III+IV paresis	Normal
6	M	65	R	Traumatic	Moped accident	30 Horner s synd 60 Exophthalmos	+	+	+	0 25	Slight diplopia	Venous stasis blurred disc
7	M	16	L	Traumatic	Moped accident	7	+	+	+	0 5	VI paresis	Venous stasis blurred disc
8	M	54	R	Traumatic	Bicycle accident	30	+	+	+	1 0	Impaired movements	Venous stasis slight oedema
9	M	22	L	Traumatic	Car accident	1	+	+	+	0 67	Impaired movements	Slight venous stasis
							+	+	+	1 0	VI paresis → −	Slightly blurred disc

Exophthalmos had been present in 14 patients Within a week after operation it disappeared completely in 10 (13 eyes) and abated to some extent in two These two patients did not return for follow up examination and did not answer inquiries by letter In two patients, the exophthalmos subsided, but recurred later, and in spite of several subsequent operations pulsating exophthalmos persisted, although it was less severe than before the surgical intervention (cases 5 and 15)

Oedema of the eyelid, conjunctiva and orbital region and *dilated veins* in the eyelid and conjunctiva disappeared completely in eleven and abated in four after operation

Pulse synchronous bruit disappeared postoperatively in all patients except one (Case 8), in whom it was, however, considerably less severe one week after ligation of the internal carotid artery

Vision was normal in most of the patients before operation (0 5–1 0 in nine patients — 10 eyes) No postoperative improvement was obtained in two patients (Cases 1 and 10, no light perception) Three weeks after operation improvement from no light perception to counting of fingers at 2 metres occurred in both eyes in Case 12 In Case 5, the vision improved from 0 25 to 1 0

Gradual deterioration of vision was observed post-operatively in two patients after ligation of the common carotid (Cases 6 and 15) About two years later both revealed optic atrophy and 3–4 years later vision was determined as no light perception in one and counting of fingers at 0 5 metre in the other

Ocular movements improved postoperatively in most of the patients However it should be noted that paresis of the abducent nerve persisted for several months in some cases (Table 2)

The retinal changes resolved or abated postoperatively in most eyes However it is worthy of note that in Case 2 transient venous stasis and retinal oedema developed after ligation of the internal carotid, and that considerable aggravation with increased venous stasis and papilloedema accompanied by numerous haemorrhages and tiny cotton wool exudates was observed after ligation of the common carotid in two patients (Cases 6 and 15) Ophthalmodynamometry revealed a reduced pressure in the ophthalmic artery in the older of the two patients Two years later optic atrophy accompanied by severe visual impairment had developed in both cases

Pre operatively *corneal sensibility* was lost in one patient and impaired in two In Case 1 anaesthesia of the cornea and of the first branch of the trigeminal nerve persisted after operation In the other two patients the corneal sensibility was normal at the follow up examination Postoperative corneal hypaesthesia developed in two patients (Cases 6 and 15)

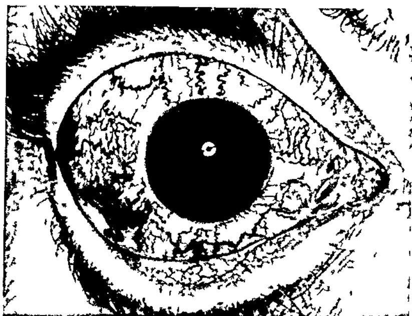


Fig 7
Conjunctival changes in a 26 year old man with right sided fistula (Case 15)

Most of the patients had noticed *diplopia*, and all had limitations of ocular movements Paresis of the abducent nerve was present in seven, of the abducent and oculomotor nerves in two, and complete loss of ocular movements was observed in eight

Corneal sensibility was lost in one patient and impaired in two

Ophthalmoscopy revealed a normal fundus in seven eyes, while venous stasis and/or slight papilloedema were present in 11 One patient with spontaneous carotid cavernous fistula (Case 1) had extensive retinal haemorrhages, which resolved postoperatively, but then a glaucomatous cupped disc was observed Case 10 had a large vitreous haemorrhage after a direct trauma to the eye sustained a few months before, when a badminton ball had hit his eye

One patient had absolute *glaucoma* In four patients, the intra ocular pressure had been measured before operation, and it was increased in all four (6–7 mm Hg higher than in the opposite eye) In two of these patients, the tension was measured postoperatively, it had then decreased to normal values in both cases, Rubeosis iridis was observed in one patient (Case 6)

Surgical Treatment

Operation was performed in 15 patients, and an account of the effect on the individual signs is given below

Table 2 shows the surgical procedures applied and their effect as assessed at the last follow up examination

11	Internal carotid ligation	+	2 months	?	VI par s	Normal
12	Muscle embolisation and internal carotid ligation	RE +		Fct 2 m	VI paresis	Normal
		LI +	3 weeks	1 ct 2 m	III+VI paresis	Normal
13	Spontaneous thrombosis of cavernous sinus	+	3½ years	0 5	Normal	During cavernous thrombosis severe retinopathy after 3½ years senile macular degeneration
14	Internal carotid ligation later trapping later external and common carotid ligation	+	3 years	1 0	Normal	Normal
15	Common carotid ligation later internal carotid ligation followed by trapping and stepwise ligation of arteries (external carotid superior thyreoid dorsal nasal supraorbital and superior palpebral arteries)	(+)(exoph bruit)	3 years	I ct o 5m	Normal	Retinopathy had aggravated later atrophy of the optic disc
16	Muscle embolisation by the method of Hamby (1966)	+	1½ years	0 67	VI paresis	Normal
17	No treatment		4½ months	1 0	VI paresis	No change
18	No treatment — the patient died after a few days		Dead	?		

Table 2

Data after treatment at the last control

Treatment	*Effect on pulsation exoph , brut*	*Follow up*	*Visual acuity*	*Motility*	*Fundus*
1 Common carotid ligation	+	8 years	No LP	Severely impair ed movements	Glaucomatous cupped disc
	RE +		1 0	Slight VI paresis	Normal
2 Internal carotid ligation later trapping	LE +	5 months	1 0	Normal	Normal
3 Common carotid ligation later internal carotid ligation					
4 Internal carotid ligation	+	3½ years	1 0	Normal	Normal
	+	4 years	1 0	Normal	Venous stasis and oedema — normal
5 Common carotid ligation later ligation of internal carotid later trapping and orbitotomy	(+)(exoph)	10 years	1 0	Normal	Normal
6 Common carotid ligation	+	4 years	No LP	Total VI paresis	Retinopathy had aggra vated, later atrophy of the optic disc
7 Internal carotid ligation	+	3½ years	1 0	Normal	Normal
8 Internal carotid ligation	(+)	1 week	0 67	Diplopia	No change
9 Internal carotid ligation	(+)	1 week	1 0	Normal	No change
10 Common carotid ligation later internal carotid ligation	RE +	Dead after	No LP	?	Normal
	LE +	8 days Dead after	No LI	?	Vitreous haemorrhage

Discussion

It is noteworthy that in two cases of this series, ligation of the common carotid artery was followed by distinct aggravation of the venous stasis and haemorrhages and cotton wool exudates in the fundus These changes were also present in the patients at a follow up 4–5 months later In the other surgical patients, the venous stasis and papilloedema regressed shortly after the intervention

Patients with carotid cavernous fistula are marked by greatly blood-filled veins, and it should therefore be expected that ligation of the afferent artery would result in cessation of the venous stasis This, in fact, also occurs in most cases, but some examples are on record in which ligation of the common or internal carotid has led to aggravation of the retinopathy (Knapp 1901 Ruata 1916, Augstein 1916 Jaensch 1924 Swans and Raaf 1951, Schenk 1955, Holst (Case 2) 1960 Renpenning and Wacasar 1963, Mooney 1965 Sanders and Hoyt 1969)

The development of this retinopathy may have several causes In the German literature special emphasis is placed on the similarity to Purtscher s retinopathy which is referable to a suddenly increased venous pressure after head or chest injuries In his two patients *Schenk* (1955) explained the retinopathy as a consequence of a recurrence of sudden onset. Other authors e g Swan and Raaf (1951) expressed the view that venous stasis and retinopathy were consequences of arterial hypotension and Sanders and Hoyt (1969) also emphasised that hypoxia is an essential factor in the development of the ocular manifestations in carotid cavernous fistula and that surgery may very well increase this hypoxia Stern, Brown and Alksne (1967) pointed out that cerebral hypoxia mainly occurred after ligation of the carotid in the neck alone If it is this arterial hypotension which is the cause of the aggravation of the venous stasis and retinopathy it must be of the same nature as that seen on occlusion of the carotid artery (Kearns and Hollenhorst 1963) and the ophthalmic artery (Madsen 1966)

The two patients in the present series with pronounced aggravation in the ophthalmoscopic appearance had in fact several signs of hypoxic ocular disease

One of the patients had, although he was only 26 years old a slightly increased blood pressure and the other aged 65 had arteriosclerosis In both cases diminished corneal sensibility was observed after operation and gradual impairment of vision occurred The older of the two patients lost light perception and in the younger vision was reduced to counting of fingers at 0 5 metre after three years Ophthalmoscopy performed 4–5 months postoperatively revealed the persistence of mild papilloedema venous stasis haemorrhages and exudates The retinopathy with several

Ophthalmodynamometry was performed in five patients postoperatively The pressure in the ophthalmic artery was reduced to from one third to one half of normal on the side subjected to operation, but no definite correlation between the pressure in the ophthalmic artery and visual acuity was observed The lowest diastolic pressure (10 *mm* Hg) was measured in Case 5, who had preserved a vision of 1 0

The *treatment* applied in the 15 cases appears from Table 2 Ligation of the internal or common carotid was performed in seven cases, which resulted in subsidence or complete disappearance of exophthalmos In another six patients the primary ligation of the internal or common carotid had to be supplemented by further ligations A good result was obtained by primary muscle embolisation of the fistula in two patients (Cases 12 and 16) In Case 12, a silver-clipped muscle strip was introduced through the internal carotid into the fistula by means of an embolectomy catheter (Prof Malmros) In Case 16, ligation of the internal carotid was performed intracranially, with introduction of a muscle embolus into the interal carotid and ligation of the common, internal and external carotids in the neck (Dr Husby) Postoperative radiography showed that in both cases the muscle embolus was at a level with the fistula Case 16 will be published elsewhere (Olsen 1969)

In one patient (Case 5), epilepsy developed after several operations on the vessels in the neck and intracranially The operations did not give rise to severe hypoxic cerebral lesions in any of the other patients

No Treatment

No treatment was given in three patients One died after a few days in hospital (Case 18) In another, the condition was unchanged after the lapse of 4½ months (Case 17) The third patient was a 72-year old woman in whom left sided carotid cavernous fistula developed, after head injuries with fracture of the skull (Case 13) Three weeks later, thrombosis of the cavernous sinus led to fever and increased protrusion of the left eyeball In connection with the increased protrusion the pulse synchronous bruit ceased There was transient aggravation of the retinopathy with disc swelling, markedly dilated veins and flame shaped haemorrhages The symptoms of the thrombosis of the cavernous sinus resolved within a month, and so did the signs of carotid cavernous fistula In this patient with a typical carotid cavernous fistula, spontaneous thrombosis of the cavernous sinus resulted in closure of the fistula

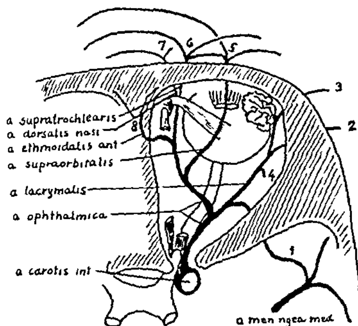


Fig 8

Anastomoses between the ophthalmic artery and the external carotid artery

1 Recurrent meningeal branch of the lacrimal artery to the middle meningeal artery

2 Zygomatico-temporal branch of the lacrimal artery to the anterior deep temporal artery which arises from the internal maxillary artery

3 Zygomatico-facial branch of the lacrimal artery to the transverse facial artery from the superficial temporal artery

4 Branch from the lacrimal artery to the infra-orbital artery from the internal meningeal artery

5 Supra-orbital artery anastomoses with the supra-orbital artery of the other side the supratrochlear and the superficial temporal arteries.

6 Supratrochlear artery anastomoses with the supra-orbital and the superficial temporal arteries as well as the supra trochlear artery of the other side

7 Dorsal nasal artery anastomoses with the facial artery and the artery of the other side

8 Anterior ethmoidal artery gives off the anterior meningeal artery which anastomoses with the middle meningeal artery

Figure 8 is a diagrammatic representation of the ophthalmic artery with the anastomoses to the internal and external carotid arteries Of great importance is the communication between the middle meningeal and the lacrimal arteries The ophthalmic artery is sometimes supplied mainly or exclusively by this route (Hayreh and Dass 1962, Hayreh 1962 Walsh 1957 Jamieson 1964) Most of the other communications are narrow but may if need be take over the blood supply to the ophthalmic artery and the eye After spontaneous thrombosis of the internal carotid,

small haemorrhages, red points and a few cotton wool exudates was more reminiscent of that described after occlusive vascular disorders than of the more violent exudative picture which is often observed in Purtscher's retinopathy (*Madsen* 1965, 1966) Optic atrophy was present in both patients 3–4 years later

In these two patients, who had pre-existing arterial disease, ligation of the common carotid artery had resulted in severely reduced blood supply to the ophthalmic artery

In some cases, the aggravated retinopathy may, in addition to arterial hypotension, be referable to thrombosis of the cavernous sinus and the orbital veins In Case 13, spontaneous closure of the fistula occurred after a cavernous sinus thrombosis, which was followed by retinopathy of an appearance as that seen in central-vein thrombosis

Until recently, treatment of carotid cavernous fistula consisted mainly in ligation of the common or internal carotid artery in the neck This procedure was also used in 13 patients in the series considered here This primary ligation was satisfactory in seven cases, but in the other six it had to be supplemented by other measures Ligation of the common carotid seems particularly to be insufficient as the only procedure It must be assumed that the unsuccessful surgical results were due to the presence of well developed anastomoses to the cranial portion of the internal carotid The most important communication is the circle of *Willis*, which is supplied from the contralateral internal carotid and from the basilar artery Other anastomoses between the internal carotid and the basilar artery may occasionally be present, viz primitive vessels (trigeminal and hypoglossal arteries) which have not been obliterated after the development of the posterior communicating artery In the cavernous sinus, the internal carotid gives off several small vessels which anastomose with the contralateral internal carotid and with external vessels, such as the middle meningeal artery The lack of success of repeated operations in Case 5 was possibly due to the presence of some of these vessels

Furthermore, a considerable part of the blood supply to the upper portion of the internal carotid may come from the external carotid through the ophthalmic artery This is one of the reasons why, in intracranial ligation of the internal carotid (trapping operation), an attempt is made to place the ligature caudalward to the origin of the ophthalmic artery, or why it may also be necessary to ligate this vessel In some patients, the ophthalmic artery can be ligated at the origin *without* causing blindness of the eye This can be done only because of the presence of wide anastomoses to the external carotid The ophthalmic artery is an "arterial bridge" with well developed communications to both the internal and external carotids (Rushede 1957, Krayenbuhl and Yasargil 1965)

aggravation of the retinopathy and subsequent optic atrophy, probably due to hypoxia, were observed in two cases

Vision was unchanged in 11 patients after operation, improvement occurred in two and deterioration in two

Spontaneous thrombosis of the cavernous sinus with closure of the fistula occurred in one of the patients who were not subjected to operation A saccular carotid aneurysm was observed in one of the patients with fistula of spontaneous origin

Owing to the numerous possibilities of anastomoses, ligation of vessels had to be repeated in five cases in order to obtain an acceptable result Accordingly, it is desirable to perform a direct operation on the fistula at once

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such anastomoses between the external carotid and the ophthalmic artery are often observed In such cases, angiography of the common carotid reveals an occlusion of the internal carotid artery, but filling of the external branches, and through the ophthalmic artery, also of the carotid siphon and the intracerebral vessels (Riishede 1957, Riishede, Ottosen and Sondergaard 1960, Jacobsen and Skinhoj 1957) However, Riishede (1957) reported that the communications between the external carotid and the ophthalmic artery were established through the internal maxillary artery, not through the *facial or middle meningeal arteries*

In view of all these possibilities of the formation of anastomoses, it is not surprising that operation on the cervical vessels alone may be followed by recurrence *At subsequent operations, such anastomoses may have formed*, and it may be necessary to ligate vessels, one by one, in successive operations without achieving closure of the fistula, as was seen in two patients of the present series (Cases 6 and 15) Better procedures are (1) the trapping operation with simultaneous ligation of the internal carotid both in the neck and intracranially, preferably in such a way that the ophthalmic artery is spared, or (2) muscle embolisation in combination with ligation of the internal carotid artery Furthermore, as emphasised by Sanders and Hoyt (1969), a pre operatively increased intra ocular pressure should presumably be reduced in relation to the ligation of the carotid vessels Otherwise, a disproportion between the high intra ocular pressure and the low pressure in the arteries after the ligation may easily arise, and this may lead to serious consequences, especially in the presence of pre existing arterial affection

Summary

A study on a series of 18 patients with carotid cavernous fistula is presented *Of the cases, 16 were of traumatic origin, while two were of* spontaneous onset One patient had bilateral fistulae In the remaining 17 patients, the fistula was unilateral, but three of these patients had bilateral manifestations

Thirteen patients were treated with ligation of the carotid vessels, and two with ligation and muscle embolisation Lasting effect on the pulsating exophthalmos was obtained in 11 patients, in two the effect was incomplete in spite of repeated operations Two patients did not return for follow up examination

Bruit disappeared in all patients but one There was also improvement of the eye movements in most patients

The retinal changes disappeared in most of the cases Postoperative

ophtalmica sin to be filled with a cohesive somewhat whitish thrombus formation attached to the wall and very brittle The frontal sinuses were clear on both sides. There was a considerable injection of the middle cranial cavity particularly above the cavernous sinus and down the lateral wall to the sphenoidal bone The intercavernous sinuses were also full to the brim of thromboses

Conclusion from section A conclusive cavernous sinus thrombosis on a septic foundation with localized basal meningitis The thrombosis began on the left side and spread to the right through the intercavernous sinuses

Six years ago a similar case was admitted to the Department a 34 year-old man with initial shock from a nasal furuncle who recovered after intensive antithrombotic and antibiotic treatment.

I have personally seen a total of 4 such cases all men. In 1936 400 cases of cavernous sinus thrombosis were collected from all over the world all mortal In 1937 the first case was successfully treated with sulpha Anticoagulation treatment was first introduced in 1941 by Lyons(1) The first case to be completely cured with penicillan was described by Goodhill(2) in 1944

In 1948 the literature of this complaint was supplemented by 60 cases of documented cavernous sinus thrombosis 53 patients of 88% recovered although only 23% of these without serious complications or residual abnormalities. These cases were presented by Shaw(3) who states that this degree of comparative restitution is on the whole unduly high

The primary foci of infection were Furuncles on cheeks forehead nose lips and eyelids Also sinusitis with nasal infection, otitis dental infection facial injuries and in a small number of cases more remote infection.

The sequelae were Amaurosis ophtalmoplegia ptosis and atrophy

The solution is diagnosis at the earliest possible moment and only a combination of antibiotic and antithrombotic treatment started at an early stage can save the patient Diagnosis cannot always be left to more refined and sophisticated special examinations but must be made at the bedside as early as possible by an experienced specialist.

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Discussion

T Waalen (Gjøvik)

CAVERNOUS SINUS THROMBOSIS

When one has followed for decades the positively explosive developments in the special fields of medicine, not least in opthalmology, one cannot help being struck by the wealth of material put forward in the course of these few days concerning the orbit and neuro opthalmology

We have heard that the orbit has no lymph tracts that its venous channels are not supplied with valves, and that they drain into the cavernous sinus via the vena ophtal mica sup and posterior If there is good communication between the vena angularis and the vena opthalmica infectious processes from the nose and facial region will be able to spread easily and quickly to the orbit and to the cavernous sinus

What will this mean for clinical practice and for the future? It seems likely that the increasing number of head injuries, with open lesions in the skin and mucous mem brances, will lead to such serious processes becoming more common A case admitted some months ago to the Department where I work shows how important it is that the opthalmologist enters the picture as soon as possible

Early diagnosis is a decisive factor in prognosis and it may well be the eye specialist who saves the day

A 24 year old man became suddenly ill with pyrexia, slimy secretion from the left nostril, red and swollen nose for 8–10 days On admission to the Department he had a small lesion in the left vestibule of the nose He had been treated for 3–4 days by a general practitioner with doses of penicillin On being admitted to the Department for Sinusitis he had a high temperature a red and swollen left nostril and venous stasis in the left conjunctiva In the course of the evening and night venous stasis also developed in the conjunctiva of the right eye In the early morning of October 13 1969 he became comatose and had a rectal temperature of 41 7 The eye grounds showed markedly congested veins like thick sausages no appreciable prominence or oedema of the optic discs An X ray showed clear sinuses The clinical diagnosis was cavernous sinus thrombosis and apparatus maxima was set in with 10 ml antibiotics every 4th hour Heparin 3 ml intravenous + Stremptomycin $\frac{1}{2}$ g×2 + Chloramphenicolsuccinate 1 g×4 Antiphlagistic treatment with Largactil was given the sickroom was cooled and a freeze mattress was employed

No reversal of the condition occurred and death took place at about 10 a m preceded by jerking of the arms and legs Section showed the cavernous sinus and vena

patients and one as an out patient in various clinics of the University Hospital Lund, because of extraocular and ocular symptoms One single patient lacked extraocular symptoms and was referred to us from another ophthalmologist because of blurred and elevated discs In all the cases ocular examinations were made by us one or several times Papilloedema existed in 16 patients I 9 the oedema was due to brain tumour verified by surgery, in 2 to cerebral trauma, in one to encephalitis and in one to arterial hypertension Three patients, in whom the cause of the papilloedema remained obscure, deserve special reports

Case 8 a woman of 48 had been examined in this hospital in 1956 because of headache arterial hypertension and papilloedema of 3-4 D On that occasion a brain tumour was suspected but could not be confirmed. The papilloedema decreased spontaneously over some months but did not disappear In November 1968 she was again hospitalized because of spontaneous liquorrhea A general neurological examination was negative The blood pressure was 220/120 mm Hg The visual function was normal The optic discs were blurred elevated 1 D and a little pale The retinal arteries were narrow and there were marked arterio-venous crossing defects but no haemorrhages Enc phalography did not reveal any brain tumour She was recommended further investigation but did not accept partly since the liquorrhea had disappeared after repeated lumbar punctures.

Case 19 a man of 58 was referred to this hospital because of headache arterial hypertension and papilloedema A general neurological examination was negative The blood pressure was 180/110 mm Hg The visual function was normal The optic discs were hyperaemic blurred and elevated 3 D (R.E) and 2 D (L E) The retinal arteries were narrow and the veins dilated. There were crossing defects and juxtapapillary hard exudates but no haemorrhages. The ventricular fluid pressure was normal Angiographic and encephalographic examinations did not reveal any brain tumour The patient was discharged and antihypertensive medicine prescribed. About one month later a slight regression of the papilloedema was noted.

Case 22 a woman of 51 had been suffering from dizziness for many years Repeated examinations in another hospital had been negative until 1966 when the discs were found to be blurred A carotid angiography was performed but was negative In July 1968 she was referred to this hospital A general neurological examination was negative The visual function was normal The optic discs were blurred and elevated 1 D and the retinal veins were engorged Encephalographic examination did not indicate any brain tumour and she was discharged In March 1969 the disc protrusion had increased to 3 D and small haemorrhages and exudates had appeared on the left disc Therefore a new and extensive investigation was performed in this hospital The ventricular fluid pressure was 10-20 mm Hg i e slightly increased but neuro-roentgenological examinations were still negative In spite of this, the progressive course supports the existence of an expanding intracranial lesion.

In 9 patients there was no papilloedema The changes of the optic discs were either slight or typical of pseudo papilloedema For examples, buried drusen in one disc existed in *case 1* myopia with supertraction and nasal blurring of both discs in *case 2* monocular hypermetropia with

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DIFFERENTIATION OF PAPILLOEDEMA FROM PSEUDO PAPILLOEDEMA BY FLUORESCEIN OPHTHALMOSCOPY

By

H G Bynke, M D and L Åberg, M D

The difficulties in differentiating between certain forms of papilloedema and pseudo papilloedema are well-known to ophthalmologists This problem becomes urgent in cases where other symptoms are vague or absent, since the indication for an extensive neuro roentgenological examination is then entirely dependent on a correct interpretation of the disc changes

According to Miller *et al* (1965), Jutte & Lemke (1968), Wessing (1968), and others, this differentiation may be facilitated by using fluor escein intravenously As mentioned by David *et al* (1963) various abnor malities may be found by fluorescence technique in papilloedema One of these is the 'residual' or 'deep' fluorescence of the optic discs Thus, in papilloedema the dye leaks out through the vessel walls, producing a fluorescence of the extravascular tissue of the disc which may persist for hours On the contrary, in pseudo papilloedema this fluorescence is lacking or very slight

In 10 cases with papilloedema and 10 with pseudo papilloedema, which were reported by Miller *et al* (1965) there seem to have been no excep tions to this rule Dollery *et al* (1965), who studied the disc fluorescence by quantitative methods, found that on an average, the intensity was significantly larger in oedematous than in normal discs However, in 2 discs out of 23 with oedema it was of the same size as in 10 normal discs The latter observation is of great clinical importance since the reliability of the method, among other things, must depend on the frequency of cases with true oedema, in which the fluorescence is so faint that the condition may be misinterpreted as pseudo oedema

The present pilot study was performed in order to test the reliability of the method

Material

The material consists of 25 patients, 13 male and 12 female, aged be tween 9 and 66 years (*Table*) Twenty three cases were treated as in

Table 1

Clinical data and results of fluorescein ophthalmoscopy in 16 cases with papilloedema and 9 with pseudo-papilloedema

Case No	Sex	Age (years)	Diagnosis	Type of disc change	Protrusion (Dioptres) R E	Protrusion (Dioptres) L.E	Other Qualities	Disc fluorescence R.E	Disc fluorescence L E
1	m	55	Parkinsonism	Pseudo-oedema R.E	2	0	Drusen	0	0
2	m	21	Migraine	Pseudo-oedema	0	0	Myopia	0	0
3	f	66	Glioma frontal lobe	Oedema	<1	0	——	+	+
4	f	19	Syncope	Pseudo-oedema R.E	<1	0	Constant findings 5 months	0	0
5	m	32	Cerebral contusion	Oedema	2	3	Haemorrhages	+	+
6	f	53	Carotid body tumour	Pseudo-oedema	<1	0	Constant findings 3 months	(+)	(+)
7	m	37	Art. hypertension	Oedema	2	2	Hypertensive retinopathy	+	+
8	f	48	Liquorrhea	Oedema	1	1	Regression some months	+	+
9	m	29	Subdural and intracerebral haematoma	Oedema	<1	<1	——	+	+
10	m	32	Jacksonian epilepsy	Pseudo-oedema	0	0	——	0	0
11	f	49	Cerebellar astrocytoma	Oedema	2	2	Regression 4 months	(+)	(+)
12	f	52	Glioma temporal lobe	Oedema	0	0	——	+	+
13	m	55	Glioma temporal lobe	Oedema	1	1	Haemorrhages	+	+
14	m	20	Post traumatic headache	Pseudo-oedema	1	1	Constant findings 2 months	(+)	(+)
15	f	45	Healthy	Pseudo-oedema	2	2	Constant findings 10 months	0	0
16	m	13	Epilepsy	Pseudo-oedema R E.	1	0	Hyperopia R E	0	(+)
17	f	33	Cerebellar astrocytoma	Oedema	3	3	Regression 2 months Secondary atrophy	+	+
18	f	64	Acoustic neuroma	Oedema	1	2	Haemorrhages	+	+
19	m	58	Art hypertension	Oedema	3	2	Exudates	(+)	(+)
20	m	9	Encephalitis	Oedema	3	1	Regression 1 month	(+)	(+)
21	f	64	Meningeoma parietal lobe	Oedema	2	2	——	+	+
22	f	51	Intracranial hypertension	Oedema	3	3	Haemorrhages Exudates	+	+
23	m	40	Glioma frontal lobe	Pseudo-oedema (slight)	0	0	Constant findings 2 months	(+)	(+)
24	f	33	Acoustic neuroma	Oedema	4	4	Macular oedema	(+)	(+)
25	m	47	Meningeoma parietal lobe	Oedema	2	2	Haemorrhages	+	+

ipsilateral disc changes in *case 4* and constant disc changes over 10 months without subjective symptoms in *case 15*

Because of co existing general symptoms, neuro roentgenological examinations were performed in 4 patients with pseudo papilloedema (*cases 1, 4, 6 and 10*) but were negative In one single patient (*case 23*) a brain tumour was discovered and verified by surgery before any ocular examination had been performed The very slight, nasal blurring of the discs of that case was constant over 2 months and was interpreted as a normal finding

To sum up, the diagnosis of the disc changes could be considered valid in all the cases on account of various clinical data and typical course

Method

After a complete neuro-ophthalmological examination the patient was placed recumbent with his pupils dilated by Cyclogyl 1% (Schieffelin) Three ml of Fluorescein sodium 20% (ACO) were rapidly injected into the cubital vein or into a vein of the dorsum of the hand The time after the injection was recorded by a stop watch The eye grounds were examined by means of a Zeiss Opton ophthalmoscope with a blue filter (BG_{12}) inserted, as described by Jutte & Lemke (1968) Through this filter the fluorescein appears as a greenish-yellow glow against the blue back ground

Before the injection, the dark adapted observer examined the fundi to recognise their appearance in the blue light Immediately after the injection the fundi were observed practically continuously during the first 5 minutes and then repeatedly with intervals of about 5 minutes until half an hour had passed

No important complication of the injection was observed However, 7 patients got nausea of short duration with or without vomiting This appeared 1–2 minutes after the injection and disappeared about one minute later

Observations

Between 10 and 20 seconds (av 11) after the intravenous injection the dye appeared in the retinal arteries and a few seconds later in the veins In this early phase it also filled out the superficial vascular plexus of the optic discs This was dilated in several cases with papilloedema and became very conspicuous after the injection During the following minutes the fluorescence of the retinal vessels gradually subsided A choroidal fluorescence also became more or less apparent after some minutes

Comments and Conclusions

In this study attention was mainly paid to the deep, residual fluorescence of the optic discs This was found to be much more marked in 12 out of the 16 cases with papilloedema than in the 9 cases with pseudo papilloedema Therefore, the fluorescein examination seems to be valuable for a differentiation of the two conditions This conclusion agrees with that of Miller *et al* (1965), Jutte & Lemke (1968), Wessing (1968), and others

In 4 out of the 16 cases with oedema, the disc fluorescence was faint and of the same order of size as in some cases with pseudo-papilloedema Consequently a 'negative result does not exclude the possibility of *papilloedema In the case with the faintest fluorescence the papilloedema* was of the chronic type It should be mentioned that O Day *et al* (1967) found the deep fluorescence to be absent or reduced in optic atrophy and chronic papilloedema, respectively

Sanders & ffytche (1967) reported characteristic changes after fluorescein injection in drusen of the disc Such changes were not observed in the single case in this series in which drusen existed

The disc fluorescence was found to appear about 1–2 minutes after the injection reached a maximum after 10–15 minutes and persisted for at least half an hour To recognise this phenomenon it may therefore be sufficient to start the fundus examination some minutes after the fluorescein injection Furthermore because of the reduced demand of timing the complicated photographic device may be replaced by the handy ophthalmoscopic method as in this study In a busy clinical routine, such simplifications are useful and may even be necessary

Although a photographic method would be expected to permit a more objective quantification of the disc fluorescence it should be pointed out that even that method is impaired by sources of error One important error was mentioned by Lemke *et al* (1967) on the photograph the fluorescence before the injection (the primary fluorescence) cannot be distinguished from that due to fluorescein (the secondary fluorescence)

Summary

In 16 cases with papilloedema and 9 with pseudo-papilloedema the optic discs were studied by blue filter ophthalmoscopy after intravenous injection of fluorescein The deep disc fluorescence was found to be much more marked in the majority of the cases with oedema than in the cases with pseudo-oedema However in 4 cases with oedema it was faint and of the same order of size as in some cases with pseudo-oedema

It was concluded that fluorescein ophthalmoscopy is valuable for a differentiation of the two conditions but that the method is not entirely reliable

In the cases with papilloedema, a diffuse fluorescence of the optic discs was first observed between ½ and 2½ minutes after the injection It started on a small area and gradually extended over a larger part of the disc In some cases the dye faded into the surrounding retina and after several minutes into the vitreous body The intensity of the disc fluorescence gradually increased and reached a maximum about 10–15 minutes after the injection At this point the dye had almost disappeared from the retinal vessels It was observed only in the walls of some branches This deep, residual disc fluorescence persisted at the end of the examination half an hour after the injection

The intensity and extension of the disc fluorescence varied individually but was considerable in 12 of the 16 cases with oedema (*Table*) In some cases it was even larger than might be expected from the size of the oedema For example, in *case 3*, in which there was an unmistakable but small oedema of the right disc but only a slight nasal blurring of the left, the fluorescence proved to be bright also in the left disc Therefore, it was possible to conclude, on the basis of the fluorescein examination, that the papilloedema was bilateral

In 4 cases with oedema the disc fluorescence was found to be faint *Case 11* was the most remarkable one in this respect Both discs were blurred around their margins, elevated 2 D and a little pale, but visual function was normal There were multiple, refractile bodies on the disc surface The retinal veins were engorged but there were no haemorrhages Although a chronic papilloedema was suspected, a pseudo papilloedema seemed to be possible The disc fluorescence proved to be very faint, so the condition might have been misinterpreted as a pseudo oedema But there was also a pathological nystagmus Therefore, a complete neuro roentgenological examination was performed and showed a tumour in the posterior fossa After the removal of a cerebellar astrocytoma the discs became normalized in the course of about four months, and the diagnosis of a true papilloedema could be confirmed Also in *case 20*, the papilloedema was of the inveterate type, but the subjective symptoms had only lasted for about one month In the other two patients with a faint fluorescence, *cases 19 and 24*, the oedema appeared to be of the recent type but without haemorrhages

In the 9 cases with pseudo oedema, including *case 23*, the disc fluorescence was either lacking or very faint (*Table*) Furthermore, it was usually not observed as early after the injection as in the cases with papilloedema No disc fluorescence was observed in *case 1*, in which there were buried drusen in the right disc In *case 16*, in which the pseudo oedema was unilateral, a faint fluorescence was found only in the normal disc

Comments and Conclusions

In this study, attention was mainly paid to the deep, residual fluorescence of the optic discs This was found to be much more marked in 12 out of the 16 cases with papilloedema than in the 9 cases with pseudo papilloedema Therefore, the fluorescein examination seems to be valuable for a differentiation of the two conditions This conclusion agrees with that of Miller *et al* (1965) Jutte & Lemke (1968), Wessing (1968), and others

In 4 out of the 16 cases with oedema, the disc fluorescence was faint and of the same order of size as in some cases with pseudo papilloedema Consequently, a negative result' does not exclude the possibility of papilloedema In the case with the faintest fluorescence the papilloedema was of the chronic type It should be mentioned that O Day *et al* (1967) found the deep fluorescence to be absent or reduced in optic atrophy and chronic papilloedema, respectively

Sanders & ffytche (1967) reported characteristic changes after fluorescein injection in drusen of the disc Such changes were not observed in the single case in this series in which drusen existed

The disc fluorescence was found to appear about 1–2 minutes after the injection, reached a maximum after 10–15 minutes and persisted for at least half an hour To recognise this phenomenon it may therefore be sufficient to start the fundus examination some minutes after the fluorescein injection Furthermore because of the reduced demand of timing, the complicated photographic device may be replaced by the handy ophthalmoscopic method, as in this study In a busy clinical routine, such simplifications are useful and may even be necessary

Although a photographic method would be expected to permit a more objective quantification of the disc fluorescence, it should be pointed out that even that method is impaired by sources of error One important error was mentioned by Lemke *et al* (1967) on the photograph the fluorescence before the injection (the primary fluorescence) cannot be distinguished from that due to fluorescein (the secondary fluorescence)

Summary

In 16 cases with papilloedema and 9 with pseudo papilloedema the optic discs were studied by blue filter ophthalmoscopy after intravenous injection of fluorescein The deep disc fluorescence was found to be much more marked in the majority of the cases with oedema than in the cases with pseudo-oedema However, in 4 cases with oedema it was faint and of the same order of size as in some cases with pseudo-oedema

It was concluded that fluorescein ophthalmoscopy is valuable for a differentiation of the two conditions but that the method is not entirely reliable

In the cases with papilloedema, a diffuse fluorescence of the optic discs was first observed between ½ and 2½ minutes after the injection It started on a small area and gradually extended over a larger part of the disc In some cases the dye faded into the surrounding retina and after several minutes into the vitreous body The intensity of the disc fluorescence gradually increased and reached a maximum about 10–15 minutes after the injection At this point the dye had almost disappeared from the retinal vessels It was observed only in the walls of some branches This deep, residual disc fluorescence persisted at the end of the examination half an hour after the injection

The intensity and extension of the disc fluorescence varied individually but was considerable in 12 of the 16 cases with oedema (*Table*) In some cases it was even larger than might be expected from the size of the oedema For example, in *case 3*, in which there was an unmistakable but small oedema of the right disc but only a slight nasal blurring of the left, the fluorescence proved to be bright also in the left disc Therefore, it was po sible to conclude, on the basis of the fluorescein examination, that the papilloedema was bilateral

In 4 cases with oedema the disc fluorescence was found to be faint *Case 11* was the most remarkable one in this respect Both discs were blurred around their margins, elevated 2 D and a little pale, but visual function was normal There were multiple, refractile bodies on the disc surface The retinal veins were engorged but there were no haemorrhages Although a chronic papilloedema was suspected, a pseudo papilloedema seemed to be possible The disc fluorescence proved to be very faint, so the condition might have been misinterpreted as a pseudo oedema But there was also a pathological nystagmus Therefore, a complete neuro roentgenological examination was performed and showed a tumour in the posterior fossa After the removal of a cerebellar astrocytoma the discs became normalized in the course of about four months, and the diagnosis of a true papilloedema could be confirmed Also in *case 20*, the papilloedema was of the inveterate type, but the subjective symptoms had only lasted for about one month In the other two patients with a faint fluorescence, *cases 19 and 24*, the oedema appeared to be of the recent type but without haemorrhages

In the 9 cases with pseudo oedema, including *case 23*, the disc fluorescence was either lacking or very faint (*Table*) Furthermore, it was usually not observed as early after the injection as in the cases with papilloedema No disc fluorescence was observed in *case 1*, in which there were buried drusen in the right disc In *case 16*, in which the pseudo oedema was unilateral, a faint fluorescence was found only in the normal disc

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UNILATERAL PAPILLOEDEMA IN NEUROSURGICAL PATIENTS

By

E Bruntse

In neurosurgical patients papilloedema usually is regarded as an expression of increased intracranial pressure In spite of much research little is known about the pathogenesis of this papilloedema Most theories regarding the formation of papilloedema are mechanical and are based on the fact, that the subarachnoid space of the brain and of the optic nerve are in connection with each other If the intracranial pressure increases a corresponding increase will occur around the optic nerve The central retinal artery and vein pass through the subarachnoid space just behind the eye An increase of subarachnoidal pressure is believed to result in a compression of these vessels, the vein to a greater extent than the artery resulting in venous engorgement The classic interpretation is that this venous engorgement is what causes papilloedema — choked disc There is probably no doubt that the above mentioned conditions may have something to do with the development of papilloedema, but it is only part of the explanation An essential objection is that venous engorgement would be expected to result in oedema of the retina rather than of the optic nerve head The fact that even total obstruction of the central retinal vein rarely or never results in more than about three dioptres swelling is another important objection to the theory that venous engorgement should be the only factor in the pathogenesis of the oedema

Parinaud s theory that it would be natural to regard the papilloedema merely as oedema in a part of the brain has principally been accepted by recent research workers At present attention is being paid to the vessels which nourish the papilla, i e mainly branches from the circle of Zinn Bregeat concludes in his book *L Oedeme Papillaire* that the vascular changes which are found in the oedematous papilla are similar to vascular changes in other parts of oedematous brain tissue He thinks that disturbances of circulation following these vascular changes are the cause of the oedema and that they moreover are due to disorder in a common regulation

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cranial space occupying lesion regardless of place or type may result in occasional homo as well as contralateral papilloedema Conclusions have been attempted drawn up on the basis of clinical experiences but apart from a few broad outlines it is difficult to find any essential agreement Bregeat is of the opinion that cerebral abscess and temporal incarceration of the brain rather often have more papilloedema on the same side as the brain lesion than on the other Tonnis material of 88 intra cranial tumours with unilateral papilloedema showed that tumour at the base of the brain as well as brain stem tumours often had homolateral papilloedema, while tumours of the occipital lobe comparatively often had contralateral More records have been made on asymmetric papilloedema than on unilateral Gibbs concludes on the basis of 330 cases of brain tumour with asymmetric papilloedema among other things (1) Greater choking tends to occur on the same side as the tumour (2) The incidence of homolaterally greater choking is highest among tumours of the temporal and parietal lobes (3) The incidence of contralaterally greater choking is highest among occipital tumours

Paraicz et al and Dubansky et al have investigated several hundred patients with brain tumours and papilloedema Among other things they have been interested in the asymmetric papilloedema The former is of the opinion that pontocerebellar tumours often resulted in homolaterally greater choking The latter finds that 75% of supratentorial tumours equally often resulted in contralaterally or homolaterally greater choking

It appears then that the ophthalmologist often will find himself in a difficult situation when the neurosurgeon asks for an explanation of a unilateral papilloedema This is the reason for us having taken an interest in examining the cases of unilateral papilloedema which we have had the opportunity to observe We cannot expect other results from our examination than material for comparison The patients were all admitted to the neurosurgical ward of the State Hospital in Copenhagen, and all eye examinations were carried out at the eye clinic of the same hospital During a course of 15 years from 1954–1968 55 cases of unilateral papilloedema and probable intracranial disease were registered at the eye clinic During the same period 1 291 patients suffering from bilateral papilloedema were examined i e 4 4% of the patients with papilloedema were found to have unilateral oedema Perhaps a few of the 1 291 patients were not suffering from intracranial disease but it must have been only a few so even if the percentage is not precise it still shows something about the number of cases moreover it is in agreement with what others have found

Among the 55 patients with unilateral papilloedema 27 had brain tumour 4 had brain abscess, 4 had subarachnoid haemorrhage from an aneurysm 9 patients had traumatic brain injury and 6 were found to have

mechanism Bregeat does not deprive mechanical factors in and around the optic nerve head all significance Niedermeier points out more precisely the influence of these factors by suggesting that an increase in pressure in the subarachnoid space around the optic nerve may stimulate the sympathetic nervous system so that the vessels of the papilla are affected in such a way that it causes oedema Bynke's stereophotographic investigations of pulsesynchronous level variations of the papilla of the optic nerve seem to agree with the conception, that papilloedema is caused by vascular disorders of the tissue

However the oedema may be produced it would be natural to expect papilloedema due to increased intracranial pressure to become bilateral, and so it actually does in most cases Swelling of the discs is often unequal The oedema is rarely purely unilateral Still it would be most natural to imagine, that the origin of asymmetric and unilateral oedema in most cases will be the same, only the releasing factors are more pronounced in unilateral cases A great many of the asymmetric oedemas have no doubt been unilateral at first None of the theories on the origin of choked disc exclude the possibility of unilateral oedema but do not on the other hand, provide any universal explanation of the unilaterality From clinics a number of cases which were always unilateral are known It is wellknown that oedema hardly ever develops in an atrophic papilla or in a papilla that presents alterations which are characteristic of excessive axial myopia It has long been known that any difference of the intraocular pressure on the two sides influences the development of papilloedema, hypertension restrains, hypotension promotes papilloedema Here it seems to be local conditions that are of importance Patients with Foster-Kennedy's syndrome atrophy of one papilla and oedema of the other, make out a special group, characteristic of which it is that the atrophy as well as the oedema is due to intracranial disease It is believed that in such cases, an interruption of the connection between the subarachnoid space of the brain and one of the optic nerves is of fundamental importance Under these circumstances increased pressure in the subarachnoid space of the brain will only be able to reach the optic nerve head on one side

When neurosurgical patients with unilateral papilloedema due to local conditions have been ruled out a small group remains with apparently inexplicable unilateral oedema If the diagnosis of them moreover, is uncertain, one faces the problem whether unilateral papilloedema has any diagnostic value This problem is often dismissed just by stating that it probably has not, although no one seems to be able to hide that this is a matter which little is known about

Attempts have been made to solve the problem by clinical methods, but records available on the subject are sparce According to these any intra-

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opticochiasmatic arachnoiditis No explanation as to the cause of the oedema was found in 4 cases The last patient was a child with congenital hydrocephalus A closer examination immediately showed that the unilateral papilloedema in 20 cases certainly was due to local conditions Exophthalmos, excessive myopia or a Foster-Kennedy syndrome was found In 6 cases the oedema was observed only after operation In 4 cases no signs of intracranial disease were found, all 4 patients had normal visual acuity and normal visual fields

Remaining are 25 patients with verified intracranial disease and unexplicable unilateral papilloedema 14 of these had cerebral tumour, 2 had brain abscess, 4 had intracranial haemorrhage caused by an aneurysm, the remaining 5 patients had traumatic cerebral injury

8 gliomas, 3 meningiomas, 2 abscesses, 1 intracranial haemorrhage and 3 traumatic injuries had caused homolateral papilloedema, which thus was found in 17 cases 14 of these various brain affections were located either in the frontal or in the temporal part of the brain 1 meningioma was found in the parietal lobe, another in the occipital lobe 1 subdural haematoma was inaccurately defined

2 gliomas, 3 aneurysms and 2 traumatic cerebral injuries had resulted in contralateral papilloedema, which thus had occurred in 7 cases 3 of these brain affections, 1 tumour and 2 traumatic injuries were located in the occipital lobe 2 of the aneurysms were found on the middle cerebral artery, 1 on the posterior cerebral artery The remaining tumour with unilateral papilloedema, an oligodendroglioma in the posterior and middle cranial fossa proved to have a suprasellar part with a large vessel surrounding the contralateral optic nerve, *i e*, the papilloedema was probably homolateral

1 glioma of the cerebellar vermis could be placed neither in the group of homo — nor in the group with contralateral papilloedema It is remarkable that the whole material only contained one patient with cerebellar tumour and no patients at all suffering from a tumour of the brain stem It is also striking that not one single child had cerebral tumour and unilateral papilloedema Considering our few patients it may be incidental that the mentioned groups are not represented here But it seems natural to suppose that cases of unilateral papilloedema in which the oedema quickly becomes pronounced as in fossa posterior tumours, which are especially common for children, are rather rare

By examining the description of the ophthalmoscopic pictures one notices that the papilloedema usually was moderate with a swelling of 1–2 dioptres 1 frontal glioma and 1 frontal haemorrhage resulted in bilateral oedema before the patients were operated Postoperatively bilateral oedema was found in 3 of the patients, 2 of these had been operated for

glioma respectively in the occipital lobe and the temporal lobe, the third patient for abscess in the frontal lobe

Tonometry was not performed in any of the patients and none of them were known to have glaucoma It is improbable that a difference of tension should have caused unilateral papilloedema in any of our patients although it is a possibility which cannot be ignored entirely

Nor have the neurosurgical observations resulted in any explanation as to why the papilloedema of these patients became unilateral Only one description mentions a thick tumour vessel as a possible explanation to a papilloedema on the same side

There seems to be no points of resemblance whatever between the ventriculograms made The highest measured spinal fluid pressure was 1100 — the lowest was 60 mm of water

The material was also examined concerning the occurrence of brain oedema Information about this might be of interest especially as a number of theories about the pathogenesis of choked disc relies upon the presence of brain oedema This examination has not implied a dependable result It was noticed in one third of the cases that the dura was under pressure or the brain oedematous at the beginning of the operation In a few cases it was noticed that nothing remarkable appeared above cortex. According to the diagnosis there seems to be no doubt that most of our patients must have had brain oedema

The present material is too small to allow for the drawing up of any conclusions whatsoever It can only be stated that in the examined group of 25 patients suffering from unilateral papilloedema homolateral oedema was found in 17 cases contralateral in 6 2 patients with lesions in the middle of the brain had unilateral papilloedema

15 out of 17 patients with homolateral papilloedema had lesions in the temporal or frontal lobe of the brain Only 2 tumours in the posterior part of the brain had homolateral papilloedema 3 out of 6 patients with contralateral papilloedema had affections of the occipital lobe Thus one may agree with those who are of the opinion that as a rule greater choking of the disc tends to occur on the same side as the brain affection and that especially affections in the frontal part of the brain result in homolateral oedema while occipital lesions equally often result in contralateral oedema Although unilateral papilloedema perhaps occurs with some regularity it still seems probable that for the neurosurgical diagnosis, unilateral papilloedema only exceptionally has greater value than bilateral

Summary

During a course of 15 years, 55 patients suffering from unilateral papilloedema and probable intracranial disease were admitted to the neurosurgical ward of the State Hospital in Copenhagen These patients were examined in order to determine whether the unilateral papilloedema had been or might have been of any significance for the neurosurgical diagnosis

30 cases were immediately ruled out 20 had unilateral papilloedema caused by local conditions, in 6 cases the oedema was diagnosed postoperatively, and in 4 cases no cause could be determined The remaining 25 cases include 14 brain tumours, 2 abscesses, 4 intracranial haemorrhages caused by an aneurysm, and finally 5 patients with traumatic brain lesions

17 of the 25 had homolateral, 7 had contralateral papilloedema The last patient suffered from a midline tumour

The examined material is too small to allow for the drawing up of any conclusions, but after having completed the examination, one may agree with those who are of the opinion, that as a rule there is most papilloedema on the same side as the brain affection, and that especially affections in the frontal and temporal part of the brain result in homolateral papilloedema, while occipital lesions just as often result in contralateral oedema

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Discussion

U Krause (Uleaborg)

At the University Eye Hospital in Uleåborg we have attempted to analyse the degree of protrusion in papilloedema by stereophotogrammetric methods We reckon that the degree of protrusion can be measured to an accuracy of 0 1 mm possibly to 0 01 mm by cutting the disc in slices of known thickness we obtain a clear three-dimensional conception of the form of the disc Follow up investigations are possible and changes in the form of the disc can be registered We expect that this procedure will have great clinical value

ACTA OPHTHALMOLOGICA VOL 48 1970

From the University Eye Clinic Rigshospitalet Tagensvej Copenhagen
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INCIDENCE OF SPONTANEOUS VENOUS PULSATION IN THE RETINA

By

S E Lorentzen

Spontaneous pulsation of the retinal veins is limited to one or more veins on the optic disc, with examination by ordinary direct ophthalmoscopy The venous pulsation manifests itself as a slow narrowing of the vein caliber followed by a somewhat more rapid dilation to the width the vein displays during the longest period until another narrowing sets in This form of pulsation thus differs from the arterial pulse wave

Palpation of the radial pulse simultaneously with observation in the ophthalmoscope of the spontaneous venous pulsation on the optic disc reveals that the narrowing of the vein occurs immediately before the start of the radial pulse

In the presence of choked disc no spontaneous pulsation occurs of the veins on the disc *Baurmann* (1925) for instance, found no cases of spontaneous venous pulsation among 20 patients with choked disc Within the past six months I have examined 10 patients with choked disc without finding spontaneous venous pulsation in any of these

On examining patients suspicious ophthalmoscopically of choked disc it is therefore important to note whether or not venous pulsation is present If not the question arises of the significance of this phenomenon as an indicator of choked disc In other words how often is spontaneous venous pulsation present — or ab ent — on the optic discs?

Various investigat ons have been reported in the literature concerning the incidence of spontaneous venous pulsation on the normal d sc Table 1 gives a review of these The table shows that incidences ranging from 15 to 75 per cent have been found

Material and Results

The series investigated consisted of healthy individuals examined as out patients The majority were examined with a view to refraction, while some were subjected to a general health examination including the eyes

Summary

During a course of 15 years, 55 patients suffering from unilateral papilloedema and probable intracranial disease were admitted to the neurosurgical ward of the State Hospital in Copenhagen These patients were examined in order to determine whether the unilateral papilloedema had been or might have been of any significance for the neurosurgical diagnosis

30 cases were immediately ruled out 20 had unilateral papilloedema caused by local conditions, in 6 cases the oedema was diagnosed post operatively, and in 4 cases no cause could be determined The remaining 25 cases include 14 brain tumours, 2 abscesses, 4 intracranial haemorrhages caused by an aneurysm, and finally 5 patients with traumatic brain lesions

17 of the 25 had homolateral, 7 had contralateral papilloedema The last patient suffered from a midline tumour

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Table 2

Incidence of spontaneous venous pulsation and mean intra-ocular tension in mm Hg in 172 subjects, divided into 10 year age groups

Age group	Males	Females	Males & Females	Spontaneous venous pulsation present: Right eye	Left eye	Unilat	Bilat	Venous pulsation absent	Mean intra-ocular pressure in mm Hg: Right	Left
10–19	9	13	22	18 82%	17 77%	3 14%	16 72%	3 14%	11 6	11 8
20–29	19	9	28	22 72%	19 67%	5 18%	18 64%	5 18%	12 4	12 5
30–39	4	9	13	12 92%	9 69%	33 23%	9 69%	1 8%	13 6	13 5
40–49	12	17	29	29 100%	18 62%	11 38%	18 62%	0 0%	12 6	12 6
50–59	12	26	38	31 82%	27 71%	4 11%	27 71%	7 18%	13 6	13 9
60–69	9	16	25	23 92%	22 88%	3 12%	21 84%	1 4%	14 1	14 3
70–79	3	14	17	15 88%	17 100%	2 12%	15 88%	0 0%	15 6	15 4
All	68	104	172	150 87%	129 75%	31 18%	124 72%	17 10%	13 3	13 4

Spontaneous venous pulsation present in 279 out of 344 eyes or 81%

Absent venous pulsation 65 out of 344 eyes or 19%

In 31 of the 172 subjects, or 18 per cent the spontaneous venous pulsation was present in one eye only while in 124, or 72 per cent it was bilateral In 17 of the 172 subjects, or 10 per cent no spontaneous venous pulsation was observed

Of all the 344 eyes 279 or 81 per cent showed spontaneous venous pulsation while 65 or 19 per cent displayed no such pulsation

Table 3 illustrates the incidences of spontaneous venous pulsation within each sex separately to elucidate whether the incidence of this phenomenon differs for males and females

The table shows a slightly higher incidence in the female group than in the male Venous pulsation was absent in 12 per cent of the males and 9 per cent of the females while for the whole series it was 10 per cent as stated above

Table 1
Review of the statements found in the literature concerning the incidence of spontaneous venous pulsation

Author	Year	Number of subjects examined	Spontaneous venous pulsation Number of subjects	%	Number of eyes examined	Spontaneous venous pulsation number of eyes	%
Lang & Barrett	1889				61	45	74%
Bailliart	1918	66	38	58%			
Wiart	1920	12			80	16	20%
Elliot	1922	100	46	46%	200	98	49%
Reis*	1932	123	21	16%			
Sobański	1936	80	32	40%			
Redslob	1946	180		75%			
Weinstein & Forgacs	1947	100	50	50%			
Schulte	1948	100		36%			
Lawætz	1962	277	205	74%			
Ford & Sarwar	1963	5006		14.7%			

* *states himself that the figures are minimum figures*

The series included no cases of ophthalmologic abnormalities or fairly grave refractive errors (refractions between + and − 3 D).

The subjects were examined in the sitting position by direct ophthalmoscopy in a half darkened room, using a luminous electric ophthalmoscope. Each eye was carefully examined for spontaneous venous pulsation on the optic disc.

Ophthalmoscopy was followed by slit lamp examination, and the tension of each eye was measured with an applanation tonometer.

The investigation comprised 172 subjects (344 eyes), 68 males and 104 females ranging in age from 10 to 79 years.

The results are shown in table 2, where the series has been divided into 10 year age groups. This table also gives the mean intra ocular tensions of the right and the left eye within each age group, as well as those of the right and the left eye in the total series. It is seen that spontaneous venous pulsation was present in 150 of the 172 right eyes (87 per cent) and in 129 of the 172 left eyes (75 per cent).

slightly above the intra ocular pressure, because the intravenous pressure is to "support" the intra-ocular pressure without the veins collapsing. In addition to secure the centrally directed venous blood flow a certain fall of the pressure towards the centre must take place. During the systole of the heart the intra ocular pressure rises 0 5–2 mm Hg, a rise noticed daily by applanation tonometry. If during the systole the intra ocular pressure rises to a certain level above the venous pressure the walls of the vein will be compressed, in part or entirely, with a consequent spontaneous venous pulsation. As stated above, this is only observed on the optic disc where it often is particularly pronounced at the site where the vein trunk dives into the vascular funnel.

Two explanations may be given of the fact that such a pronounced spontaneous venous pulsation as to be visible in the ophthalmoscope is only present on the optic disc. One is that the venous pressure is the lowest on the disc, and the other that the venules (and the arterioles) lie loose in the disc tissue being thus easily influenced by alterations of the intra ocular pressure with consequent variations in calibre. In the nerve fibre layer the retinal vessels on the other hand lie supported and stabilized by surrounding tissue. *Bailliart* as early as 1918 called attention to this fact which has since been borne out by *Schulte* (1948) on the basis of histological examinations.

The lower pressure in the venules on the optic disc than in those of the remaining retina has various causes. As stated above a minor fall of the venular pressure takes place in the central direction. This fall is further accentuated in the disc region the venules passing in this place from the higher intra-ocular pressure to the lower intraneural and later the intra orbital pressure. The so called Venturi effect plays a part as another cause of the lower venular pressure on the optic disc. When a liquid in a tube passes from one section of a fairly large caliber to another of a smaller caliber the flow rate increases with a consequent fall of the pressure. This is what happens on the optic disc the aggregate number of veins in the retina having a total diameter exceeding that of the few veins on the disc.

These facts in connection with the balance between the intravenous and the intra ocular pressure constitute the basis of the spontaneous venous pulsation which thus can be regarded as an ophthalmoscopic visible sign of the pressure fall in the veins of the optic disc region.

The present investigation gave the result that spontaneous venous pulsation on the optic disc was present in 81 per cent of all the eyes and 90 per cent of all the subjects (being unilateral in 18 per cent and bilateral in 72 per cent) between the ages of 10 and 79. Spontaneous venous pulsation was found to be absent in 10 per cent of normals

Table 3

Incidence of spontaneous venous pulsation for 68 males and 104 females

Age group	Males: Venous pulsation present – Right	Left	Unilat	Bilat	Males: Venous pulsation absent	Females: Venous pulsation present – Right	Left	Unilat	Bilat	Females: Venous pulsation absent
10–19	7	7	2	6	1	11	10	1	10	2
20–29	17	14	5	13	1	5	5		5	4
30–39	4	2	2	2		8	7	1	7	1
40–49	12	4	8	4		17	14	3	14	
50–59	7	5	2	5	5	24	22	2	22	2
60–69	7	7	2	6	1	16	15	1	15	
70–79	2	3	1	2		13	14	1	13	
All	56	42	22	38	8	94	87	9	86	9
%	82%	62%	32%	56%	12%	90%	84%	9%	82%	9%

As seen in the table 2, the incidence of spontaneous venous pulsation showed a tendency towards a minor rise in the two oldest age groups

The mean intra-ocular pressure was 13 3 mm Hg for the total series (344 eyes) As might be expected, the intra ocular pressure, with a single exception, rose steadily from 11 7 mm Hg in the 10—19 year age group to 15 5 mm Hg in the 70—79 year group

The 279 eyes with spontaneous venous pulsation had a mean intra ocular pressure of 13 4 mm Hg, and the 65 eyes with no such pulsation a mean pressure of 12 8 mm Hg

The mean intra ocular pressure was the same for the males and females of this series, namely 13 3 mm Hg, calculated as the mean for 136 male and 208 female eyes respectively

Discussion

This paper is only concerned with the incidence It was not intended to investigate the numerous factors which may possibly underlie the occurrence of spontaneous venous pulsation in the retina Thus, for instance, the humoral blood pressure was not measured, nor was any attempt made to estimate the pressure in the retinal veins by ophthalmodynamometry Nevertheless it seems reasonable to mention some of the factors influencing the occurrence of spontaneous venous pulsation

The retinal vein pressure is supposed to be on a level with, and usually

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From The University of Bergen, School of Medicine Department of Ophthalmology
(Head Professor *Torstein I Bertelsen* M D)

OSTEOPETROSIS FROM THE OPHTHALMOLOGICAL POINT OF VIEW
A REPORT OF TWO CASES

By

Henry Aasved

Osteopetrosis (Karshner 1926) is a descriptive name given to a disease previously known by various other names including Albers Schonberg s disease osteosclerosis fragilis generalisata, osteosclerosis congenita diffusa

It is a rare disease causing an abnormal skeletal development The osteoclastic activity normally observed as a part of the moulding process is inadequate in these patients The primarily mineralised bone tissue is not removed with normal speed, while the formation of new bone is unimpaired (Zetterstrom 1957) This results in generalized thickness of the compact bones narrowing of the marrow cavities and secondary sclerosis of the bone tissue

The cause of the disease is not known It is evident however that it is frequently hereditary The sexes seem to be equally affected and no racial preponderance has been demonstrated The disease was first recognized in live patients in 1904 (Albers Schonberg) It has been classified into four different types based on clinical and genetical observations (Schinz 1952)

Type 1 Genetically dominant clinically benign
Type 2 Genetically dominant, clinically benign in the early stages later malignant
Type 3 Genetically recessive clinically benign
Type 4 Genetically recessive, clinically malignant

The benign types whether caused by dominant or recessive traits may be discovered by chance at any age on routine X ray examination These types do not show any particular ophthalmological manifestations

Type 2 is a rare dominant form which may be benign initially but later runs a malignant course with development of a severe anaemia and optic atrophy as in type 4 (Schinz 1952)

The malignant autosomal recessive type of the disease has the greatest ophthalmological interest It gives clinical symptoms from the first

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The cause of the disease is not known It is evident however that it is frequently hereditary The sexes seem to be equally affected and no racial preponderance has been demonstrated The disease was first recognized in live patients in 1904 (Albers Schonberg) It has been classified into four different types based on clinical and genetical observations (Schinz 1952)

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The benign types whether caused by dominant or recessive traits may be discovered by chance at any age on routine X ray examination These types do not show any particular ophthalmological manifestations

Type 2 is a rare dominant form which may be benign initially but later runs a malignant course with development of a severe anaemia and optic atrophy as in type 4 (Schinz 1952)

The malignant autosomal recessive type of the disease has the greatest ophthalmological interest It gives clinical symptoms from the first

months of life It has even been demonstrated in utero by X ray examinations (Pirie 1930)

The bone changes causes an increased fracture tendency

The effect on the bone marrow leads to extra medullary blood formation with subsequent hepato splenomegally and generalized lymphadenopathy The important haematological changes are haemolytic anaemia and thrombocytopenia Immature myeloid cells and nucleated erythrocytes can be demonstrated in the peripheral blood

The anaemia is due to increased haemolysis in the reticuloendothelial system The spleen has been shown to be the principle site of destruction (Engfeldt *et al* 1955, Sjolin 1959)

The ophthalmological and neuro ophthalmological findings are secondary to changes in the cranium

Hydrocephalus is frequently reported but papilloedema has only been observed in one case (Laurell & Wallgren 1920)

Deformities of the orbit and maxilla may lead to exophthalmus (Malatesta 1954, Pietruschka 1953 and 1958, Sjolin 1959, Ellis & Jackson 1962, and others) *Narrowing of the foramina at the base of the skull may* lead to lesions of the cranial nerves causing squint, ptosis, anisocoria and paralysis of the facial muscles (Pietruschka 1953 and 1958, Sjolin 1959, Ellis & Jackson 1962, Hill & Charlton 1965, and others)

Nystagmus occurs frequently and it is probably of ocular origin

Optic atrophy is the commonest and most serious ophthalmological lesion It is due to compression of the optic nerve and blood vessels in the narrowed optic canal (Pirie 1930, Riser 1941, Wheeler 1946, Eggert 1947, Sundal 1951, Pietruschka 1958, Malatesta 1954, Sjolin 1959, Modi & Kandoth 1964, Dent *et al*, 1965, Ellis & Jackson 1962, Hill & Charlton 1965, Anand 1966, Morrow *et al* 1967, Farriaux *et al* 1967, Baird *et al* 1968, and others)

This malignant type has a very bad prognosis Death often occurs within the first year of life

The treatment of malignant osteopetrosis is often disappointing The anaemia and thrombocytopenia are in some cases improved by splenectomy (Sjolin 1959, Moe & Skjaeveland 1969) Corticosteroid therapy has been tried with variable effect (Dent *et al* 1965, Farriaux *et al* 1967, Moe & Skjaeveland 1969)

To prevent progressive atrophy of the optic nerve, decompression of the optic canal is recommended *(Ellis & Jackson 1962, Hill & Charlton 1965)*

Case reports

Two cases suffering from the autosomal recessive type of malignant osteopetrosis have been treated in the Department of Pediatrics, University of Bergen, since 1967 They are described in more detail in another publication, particularly with regard to therapy (Moe & Skjaeveland 1969)

Case 1 Female born March 1967 Birth weight 2 490 gr Length 49 cm Admitted to the Department of Pediatrics at the age of 2½ months Findings on admittance Enlarged liver and spleen anaemia and thrombocytopenia Lab tests Hb 9 1 gr pr 100 ml WBC 18 400 pr cmm Blood film showed immature myeloid cells and nucleated red cells Reticulocytes 120 per thousard thrombocytes 40 000 pr cmm Serum calcium 7 9 gr pr 100 ml Serum phosphorus 2 9 mg pr 100 ml Serum bilirubin 0 5 mg pr 100 ml ard serum haptoglobin 7 mg pr 100 ml

There was evidence of increased red cell destruction in the liver and spleen

Ophthalmological examination at the age of 3 months revealed no abrormalities When the child was 9 months old a left-sided concomitant converging squint was recorded The discs were at this time pale with sharp borders identical with those seen in bilateral primary optic atrophy The direct light pupillary reflex was normal on the right side but doubtful in the left eye

From the age of about 2½ months the patient has been treated almost continuously with Prednisone The maintenance dose (10 mg) was given on alternate days This resulted in a normalisation of the haematological picture and a satisfactory general development of the child.

The relatively good general condition signs of optic atrophy without gross deterioration of vision were regarded as indications for neuro-surgical treatment Decompression of the right optic canal was performed in the hope of preventing further progression of the optic lesion The operation was undertaken in March 1968 through a right frontal flap A marked thickening of the orbital roof and narrowing of the trabecular space was noted. Histological examination of the removed bone showed scattered haemopoietic foci

Postoperative progress was uncomplicated A year and a half after the operation the vision on the right eye is still good. She walks about without difficulty The vision on the left eye is probably limited to light perception

Case 2 Male born July 1967 Birth weight 1900 gr Length 48–49 cm Periods of fever from the age of 3½ months Admitted to Department of Pediatrics when 5 months old. On admittance he was small and pale weight 4 7 kg Length 59 cm The anterior fontanelle was slightly bulging Head circumference was normal There was marked hepato-splenomegally general lymphadenopathy haemolytic anaemia and thrombocytopenia Lab tests Hb 7 8 gr pr 100 ml WBC 33 000 pr cmm Peripheral blood film showed immature myeloid cells and nucleated red cells Reticulocytes 100 per thousand thrombocytes 30 000 pr cmm Serum calcium 8 7–6 9 mg pr 100 ml Serum iron 1 2 microgr pr 100 ml Serum bilirubin 0 4 mg pr 100 ml and serum hapto lobin 0 mg pr 100 ml

Th l fespan of the red cells was reduced and the spleen was the main site of destruct on

This pat nt was in a poorer general condition than case 1 He also came under medical care at a later stage Persistant treatment with high doses of Prednisone failed to produce compl te normalisation of the blood picture Splenectomy was undertaken

in the end of January 1968 Subsequently it was possible to reduce the steroid dosage and it was stabilized on 15 mg every other day The blood picture has later remained satisfactory, even though some degree of haemolysis and thrombocytopenia have persisted

Ophthalmological examination showed a variable divergent squint and an irregular ocular nystagmus The right pupil showed an indefinite reaction to light, while the left eye showed an amaurotic reaction There was a marked optic atrophy with pale discs in both eyes Vision was probably restricted to light perception in the right eye and amaurosis in the left eye

Owing to the poor general condition and the poor visual function in this patient, decompression of the optic canal was not undertaken

The diagnosis was confirmed in both cases by typical X ray changes with generalized osteosclerosis, thickening of the compact bone, lack of differentiation of the compact bone and marrow together with rachitic like appearance of the epiphyses (fig 1, 2 and 3)

Following Prednisone therapy there was an improvement in the rachitic like changes but not in the osteosclerosis

Both case 1 and 2 were the only children of healthy non related parents

Two other cases with the same disease have been published previously from the Department of Pediatrics, University of Bergen (Sundal 1951) They were brother and sister with healthy parents and two healthy siblings Both the affected children had seizures hepatosplenomegally and anaemia Ophthalmological examination was only carried out in one of them revealing optic atrophy One received no treatment, the other received several blood transfusions Both died at the age of 5 months

Commentary

Atrophy of the optic nerve is the most common and the most serious ophthalmological manifestation of the malignant, autosomal recessive type of osteopetrosis

In the majority of cases the clinical picture is dominated by serious general symptoms The fact that the ultimate prognosis is very poor explains why the ophthalmological symptoms tend to be understressed Blindness is however, a very real threat to those patients who survive the early childhood years

A minority of cases presents with ophthalmological symptoms and may be referred to the ophthalmologist as a case of poor vision or squint (Hill & Charlton 1965)

The optic lesion is due to compression of the optic nerve in the optic canal Decompression of this canal may be performed In the literature there are records of three patients with osteopetrosis who have been subjected to this operation One patient had only doubtful light perception left before the operation, and no improvement could be demonstrated following surgery (Hill & Charlton 1965) Two other cases are recorded where vision are described as good even two years after the operation (Ellis & Jackson 1962, Hill & Charlton 1965)



Fig 1

Roentgenograms of skull in osteopetrosis showing marked sclerosis in comparison to a normal skull (left)

Fig 2 and 3

Roentgenograms of spine and long bones showing marked sclerosis

One would therefore advocate surgical treatment in the cases where vision is good and where the general condition is satisfactory With these views in mind decompression of the optic canal was carried out in one of our cases (case 1) Vision is still good on the treated side a year and a half after the operation

Prednisone therapy has so far successfully checked the anaemia and the thrombocytopenia in the two reported cases The steroid treatment is probably the main reason why the children are still alive

Summary

Two cases of malignant genetically recessive type of osteopetrosis are described The anaemia and thrombocytopenia have so far responded successfully to Prednisone therapy Both cases showed primary optic atrophy presumably due to narrowing of the optic canals One case presented with good vision in one eye and decompression of the optic canal was undertaken The other case presented with very poor vision and surgery was considered to have little or nothing to offer

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OPERATIVE TREATMENT OF PARALYTIC STRABISMUS

By

Magnus Odland

The purpose of this paper is to give a report of some cases operated on for paralytic strabismus where muscle transplantations have been used Transplantation of extraocular muscles has not been too generally prac used The most common procedure in management of the paralytic type of strabismus is to weaken the direct antagonist by recession of the muscle or of the contralateral synergist If the paralysis is due to a lesion of the muscle itself an operation to strengthen the affected muscle by resection or tucking is indicated and is often done together with a weakening operation of the direct antagonist

Hummelsheim (1908) reported of having done transplantation as a treatment of paralysis of the lateral rectus muscle with good result He isolated the outer halves of the superior and inferior recti muscles and transplanted them to the upper and lower edges of the lateral rectus muscle in order to augment the action A number of modifications of the original technique have later been employed O Connor (1935) describes several types of operations not only for treatment of a lateral rectus muscle paralysis but also where there have been paralysis of other muscles such as superior rectus and medial rectus One method he suggested for lateral rectus muscle paralysis was to transplant the medial thirds of the vertical recti in order to reduce the adduction action of these muscles He also tried to transplant the vertical recti *in toto* Hildreth (1953) tried to obtain abduction by shifting the direction of the vertical recti muscles by approximating them by means of a loop placed temporally The results reported with the different methods applied have varied considerably

Own material

The routine management of paralytic squint at the eye clinic Haukeland Hospital is the above mentioned procedure of recession and re section In most of the cases we get good results from these operations Sometimes however, this is not so particularly in cases of complete

Table 1

Results of muscle transplantations on 10 eyes with lateral rectus muscle paralysis

Case	Age	Cause of paralysis	Deviation before operation	Abduction before operation	Duration of paralysis	Operation	Deviation after operation	Abduction after operation
Case 1	30	Skull fracture	Ca +15	Ca 30	21 months	Recession of R M R and transplantation (2 stages)	0	35°
Case 2	33	Congenital	Ca + 5	Ca 5°	28 years	Recession of R M R and transplantation (2 stages)	−6 exotropia	15°
Case 3	23	Encephalo pathia	+18	14	10 years	Transplantation	+8 esotropia	18°
Case 4	54	Brain tumor (cordom)	+23	15	2 years	Recession of L M R and transplantation (2 stages)	0	11
Case 5	61	Skull fracture	Rt eye +25	5	11½ years	Recession of R M R and transplantation (1 stage)	−5 exophoria	25°
			Lt eye +50	0	,,	Recession of L M R and transplantation (1 stage)	+3 esophoria	5
Case 6	10	Skull fracture	+15	15°	8 months	Recession of both M R and transplantation (2 stages)	+4 esophoria	19
Case 7	71	Skull fracture	+27	10	10 months	Recession of R M R and transplantation (1 stage)	0	12°
Case 8	20	Concussion	+13	18	16 months	Recession of L M R and transplantation (1 stage)	0	27°
Case 9	14½	Congenital	+ 7	5	14½ years	Recession of L M R and transplantation (2 stages)	+5 esophoria	10

paralysis of the muscle, or if a marked contracture of the direct antagonist has taken place

During the last 5 years 12 patients have been operated on for paralytic strabismus by muscle transplantation In 2 of the cases the operation was bilateral 9 patients had the Hummelsheim operation done for lateral rectus paralysis, one of these was bilateral 1 patient with a medial rectus muscle paralysis was operated on, and 2 patients had muscle transplantation done for superior rectus muscle paralysis In one of the latter the operation was performed on both eyes

The technique described by Stallard (1950) was applied on those cases who had paralysis of the lateral rectus muscle The superior and inferior recti muscles are split along the axis of the muscle fibres for about 12 mm Between one third to one half of the muscle is separated on the temporal side The strips are then sutured through buttonholes to the lateral rectus at its insertion On all these patients except one, recession of the medial rectus was done In 5 patients this was done prior to the transplantation On all other patients it was done together with transplantation in one stage The data and results concerning these patients are shown in the table Except for one patient (case 2) all had a compensatory head posture with the head turned in the direction of the affected muscle After operation this symptom disappeared except in case 3 who still had slight deviation to the left paretic side but this did not cause him any trouble Cases 4 5 and 7 experienced diplopia in periods after the operation when looking straight forward but they were not bothered with it Almost every patient noticed some degree of diplopia when turning the gaze in the direction of the paralyzed muscle Fig 1 shows the compensatory head posture in case 1 before operation and the abduction gained after operation (Fig 2) The Hess screen tests are shown on Fig 3 and Fig 4 Fig 5 shows his field of binocular fixation before and after the operation Case 5 had considerable contracture of the medial recti as shown in Fig 6 This man had an accident 11 years ago and got a bilateral abducens paralysis The right eye had only slight movement to each side and the left eye was fixed in a maximal adducted position In order to see straight he had to turn his head about 20 degrees to the right Fig 7 shows the result of the operation He had only slight double vision in periods

The one patient who was operated on for medial rectus muscle paralysis was a 23 year old man In 1956 he had a resection done of the medial rectus muscle and also recession of the lateral rectus muscle By examination in August 1968 there was still 15 degrees divergence and he was able to adduct the eye only to the midline A muscle transplantation was then performed and the inner thirds of the vertical recti muscles were transplanted to the insertion of the medial rectus There was however little

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Case 5	61	Skull fracture	Rt eye +25	5	11½ years	Recession of R M R and transplantation (1 stage)	−5 exophoria	25°
			Lt eye +50	0		Recession of L M R and transplantation (1 stage)	+3 esophoria	5
Case 6	10	Skull fracture	+15	15	8 months	Recession of both M R and transplantation (2 stages)	+4 esophoria	19
Case 7	71	Skull fracture	+27	10	10 months	Recession of R M R and transplantation (1 stage)	0	12
Case 8	20	Concussion	+13	18	16 months	Recession of L M R and transplantation (1 stage)	0	27
Case 9	14½	Congenital	+ 7	5	14½ years	Recession of L M R and transplantation (2 stages)	+5 esophoria	10

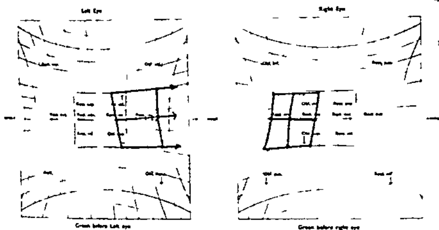


Fig 3
Case 1 Hess screen before operation

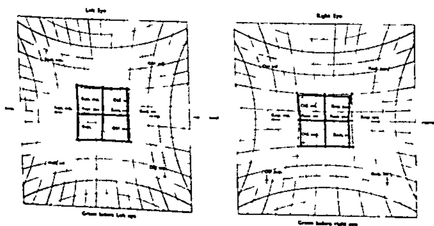


Fig 4
Case 1 Hess screen after operation



Fig 1
Case 1 Compensatory head posture in R lat rectus paralysis



Fig 2
Case 1 Abduction gained after muscle transplantation



Fig 6
Case 5 Marked contracture of the medial recti after bilateral abducens paralysis



Fig 7
Case 5 Eyes are straight after muscle transplantation

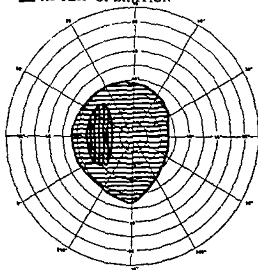


Fig 5
Case 1 Binocular field of fixation before and after operation

improvement In May 1969 a new resection and recession was done After this operation the eyes were almost straight in the primary position, but little adduction was gained He had no binocular function As already mentioned we also operated on 2 patients for defective elevation A 27-years old woman had an accident when she was 3 years old, and since then she was bothered with double vision This she compensated by abnormal head posture On examination in 1967 the left eye had 15 degrees convergence and a hypotropia of 8 prism diopters She could not elevate the eye above the midline In September 1967 she had a muscle transplantation done, and a strip from each of the medial and lateral recti muscles were moved to the insertion of the superior rectus, and the medial rectus was recessed After this operation she got hypertropia of the same eye About a year later the inferior rectus muscle was resected, and since there also was 13 degrees convergence, the same procedure was performed on the lateral rectus This gave a satisfactory result, and the diplopia disappeared

The other case with defective elevation was a 4 years old girl (Fig 8) The condition was congenital, bilateral and she also had ptosis As seen on the figure the head posture was grotesque She had first an operation for ptosis by Friedenwalds technique Afterwards muscle transplantation was performed with the same technique as described above As seen on Fig 9 there was no longer compensatory head posture She was able to elevate the eye 5–10 degrees above midline, but there was still a slight degree of ptosis left

Discussion

As to the time when surgery should be done on an acquired paralytic strabismus different views are held Some surgeons (O Connor 1935 and Gifford 1940) feel that if there is no improvement of the paralysis after 3 months, the prospect of spontaneous cure is too slight to warrant much more delay because of danger of contracture Others (Spaeth 1953 and Urist 1968) think that a period of at least a year should be allowed to elapse before operative treatment should be considered A careful examination of the ocular movements, measurement of the angle of deviation in various directions of gaze examination on the Hess screen or its equivalent and an assessment of the state of binocular function is necessary to follow the development of a possible onset of contracture or improvement

Congenital ocular paralysis should be operated on early at least where the strabismus is compensated by abnormal head posture in order to avoid structural changes in the cervical column

Complications following muscle transplantations are rare Stucchi and Bianchi (1957) and Girard and McNeely (1958) reported observing subacute iridocyclitis in a few patients in whom this operation had been done on a lateral rectus muscle paralysis All four recti muscles had been operated on in one stage Forbes (1959) reported a case which developed keratitis and the patient got an irregular pupil The complication was thought to be due to ischemia of the anterior segment of the eye This may be interpreted as a recommendation for two stage operation We did not see any complications in our patients, not even in those who had the operation done in one stage

Many are afraid to operate on an eye with a muscle paralysis, especially where there is a certain degree of deviation because of the risk of developing diplopia or make a persistent diplopia more annoying The reason for this should be that it is more easy to suppress a peripheral image than a central one If the binocular function however is well preserved, or one is able to stimulate the fusional power, the chances for gaining a satisfactory result are good Also if the paralysis has lasted for a long time, even grown up people may be able to suppress one image to a certain degree so that they will not be bothered by double vision if there is a rest deviation left Prism glasses may be indicated if diplopia persists

Summary

The most common way of treating paralysis of the external ocular muscles operatively is to weaken the direct antagonist or the contralateral synergist or both by recession of the muscles, if there still is left some



Fig 8

Grotesque compensatory head posture caused by bilateral superior recti paralysis and ptosis



Fig 9

Normal head posture gained after muscle transplantation and operation for ptosis

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From The Department of Ophthalmology Ullevål sykehus University of Oslo
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CORNEAL SENSIVITY BY LOW TEMPERATURES

By

Albert Kolstad

Every person wearing contact lenses will agree that the lenses give him least discomfort in the cold season

In the summer he must gradually build up adaptation to the lenses before they can be worn all day If they are not used daily adaptation will diminish In the winter on the other hand he can wear lenses full time without being adapted as long as he is out in the cold This fact is being exploited by week end skiers who are bothered by fogged eye glasses but do not have the motivation for daily use of contact lenses

The causes for the increased tolerance at low temperatures can only be suggested

1 A reduction in epithelium metabolism compatible with the reduced supply of oxygen
2 A normalisation of an increased temperature underneath the contact lens
3 A reduction of corneal sensitivity

Corneal sensation has traditionally been limited to that of pain and cold The pain sense is served by free nerve endings terminating in the corneal epithelium (von Frey 1894) while the cold sense is said to take its origin in Krause bodies located near the corneal limbus (Strughold & Karbe 1925)

The sensation of touch has more recently been added to the modalities experienced by the cornea (Nafe & Wagoner 1937 Lele & Wedell 1956) although the difference between touch and pain may only be one of stimulus intensity

A sensation of heat is still disputed Kenshalo and Nafe (1963) suggest that the temperature sensation originates in free nerve endings terminating on the vessel walls which in the case of the cornea would have to be the limbal vessels

The discomfort experienced by contact lens wearers has been described as being related both to the sensation of touch pain and heat

function of the paralysed muscle Resection of the paralysed muscle can in certain types also be of value If the paralysis is almost complete, muscle transplantation can offer a good alternative A report is given of muscle transplantations performed on 10 eyes with lateral rectus paralysis, 1 with a paralysis of the medial rectus and 3 with a paralysis of the superior rectus muscle The results obtained were satisfactory cosmetically, and in most of the cases also functionally Where there was fusion, the field of binocular fixation increased Where the fusion tendency was poor or not present, the patients did not complain of any disturbing diplopia No complications were observed after the operations

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mechanism Stimulus intensity is given in mg, transcribed from monofilament length using a calibration table supplied with the instrument The esthesiometer was supported against the upper part of the lamp house Since this was always placed on the left side of the microscope the subject was asked to look up to his right The monofilament was then advanced perpendicularly towards the cornea midway between apex and limbus in the 6 o clock position Stimulation was started at the lowest stimulus intensity touching the cornea between five and ten times If less than half the number of applications was felt the intensity was increased by shortening the monofilament by 5 mm and stimulation was repeated The intensity level at which the subject responded to more than 50% of the stimuli was considered threshold (Millodot & Larson 1969)

Results

The following are typical values from 50 separate measurements

Ambient temperature	Corneal temperature	Sensitivity
+22 C	+32 C	12 mg
− 6	+26	75
−14	+24	100
−16 wind	+17	100

Discussion

Brændstrup (1952) demonstrated that a person coming in from an outside temperature of −1 5 C had a corneal temperature of 21° This is a more pronounced fall than shown in table 1 This can probably be explained by the present investigation being carried out indoors where heat loss by radiation is negligible It was always a source of surprise to enter the cold room and read the air thermometer which showed a temperature much lower than common outdoors experience would indicate Schwartz (1965) measured 27 5 C on the rabbit cornea when room temperature was +3 6 C Other references to corneal temperature in a cold environment have not been found

We must therefore consider the results obtained as rather conservative estimates while the actual corneal temperature outdoors may be lower

Measurement of corneal sensitivity requires a subject sufficiently trained in the procedure to have reduced the natural reaction of anxiety to a minimum If the examination is taking place at uncomfortably low temperatures this also reduced the availability of subjects I have therefore performed the measurements on only two persons

The present investigation will be limited to the sense of touch as examined by the esthesiometer and subsequently termed the corneal sensitivity

Maximum sensitivity is found in the central part of the cornea, de creasing towards the periphery (Boberg Ans, 1955) A contact lens is today mostly fitted with apical clearance and touches the cornea with its periphery approximately mid-way between the corneal apex and limbus We shall therefore concentrate our attention on the sensitivity of this area

Methods

The two subjects investigated have normal corneal sensitivity and do not wear contact lenses The examination took place in a cold room where the temperature could be varied between —5 and —15°C Cooling of the cornea could be further increased by an artificial wind source with a wind speed of 5 m/sec

The temperature of the corneal surface was measured mid way between apex and limbus in the 6 o'clock position at least five minutes after topical anesthesia with 0 4% oxybuprocain The measurement was performed with a Mavotherm electronic thermometer working on the principle of a thermistor placed in an unbalanced bridge The instrument had a built in correction for change of battery voltage, and was found to calibrate with a mercury thermometer within one degree, which was the accuracy of the scale By low ambient temperatures the glass probe accumulated a certain amount of cold, which tended to give a lower corneal reading This could be avoided by letting the probe equilibrate with the tongue of the examiner immediately before measurement, bringing the probe into the temperature range of the cornea

Cooling of the cornea could also be obtained without a cold room by applying solid carbon dioxide wrapped in moistened cloth on the closed eyelid, by circulating an air stream through a solid carbon dioxide-alcohol mixture and directing it against the eye or by continuously dripping Hanks solution at 4°C against the open eye By all these means it was possible to produce corneal temperatures similar to those measured in the cold room

The corneal sensitivity was examined on the eye which had not re ceived local anesthesia The subject was seated in the slit lamp, and the microscope set at 6 X magnification It was found advantageous to use angled oculars which allowed comfortable change between direct (unaided) and microscopic observation

As stimulus was used a Cochet and Bonnet esthesiometer where the length of a nylon monofilament can be varied using a rack and pinion

Millodot M and *Larson W* New measurements of corneal sensitivity a preliminary report, Amer J Optom *46* 261–265 1969
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Discussion

H Forsius (Uleaborg)

On examining Lapplanders and Eskimoes who are exposed to great extremes of climate I have often seen in elderly individuals a haziness of the epithelium at the limbus of the cornea with in extreme cases a band shaped keratitis which may lead to a partial loss of sight It would be interesting to hear whether the sensibility of the cornea in this respect was investigated by the lecturer in connection with his low temperature studies.

A Kolstad

The limbus corneae has a higher temperature than the central part but in the case of a tear-drop collecting on the lower lid margin may reach 7 C and will then be completely anesthetic to touch This could explain the location of epithelial damage to the inferior limbal area in cross-country skiers (Kolstad and Opsahl 1969) but would probably not explain the bandshaped distribution of opacities seen in natives of the Arctic The mechanical trauma inflicted by snow and wind would perhaps be a more likely cause

Kolstad A and Opsahl R jr Cold injury to corneal epithelium A cause of blurred vision in cross-country skiers Acta Opthal 47 656–659 1969

The results have been the same in both persons and in all measurements performed a reduction in corneal sensitivity at the temperatures commonly found outdoors in Norway during the winter The results have been the same whether the cooling of the cornea have been caused by being in a cold room, directing a cooled air stream against the eye, dripping a cold solution on the eye, or applying a cold pack to the closed eye lid

Is the observed reduction in sensitivity sufficient to explain that contact lenses are causing less discomfort in the winter time? Boberg Ans (1955) and Byron and Weseley (1961) have, among others, shown that adapted contact lens wearers have a moderate hypoesthesia of a similar magnitude It has also been shown that persons who have not been able to adapt to contact lenses because of discomfort have a sensitivity which is higher than normal (Schirmer, 1963)

Recent work by Feldman, Flanary, Bruechert and Sampson (1969) has seriously challenged the theory that adaptation to contact lenses is explained by an increased tolerance to hypoxia We may therefore have to look for other theories A reduction in corneal sensitivity is certainly a nice theory, if for no other reasons than its simplicity As an explanation of the increased tolerance to lenses during the winter it may even be the right one

Summary

Exposure to ambient temperatures common in Norway during the winter is found to decrease the corneal sensitivity as measured by an esthesiometer It is thought that this may explain the higher tolerance to contact lenses experienced during the cold season

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Fig 1
Wheel like formation with radiate folding of the macula in a case of X-chromosomal retinoschisis

pigmentation (Fig 10) In the schisis area the retinal function is reduced which results in more or less pronounced visual field defects According to some investigators these defects correspond to the extension of the process while others maintain that some function remains in the area involved

Our studies on X chromosomal retinoschisis started in 1962 with the description of a family with this disease (Forsius *et al* 1962) Up to now we have collected 170 cases of retinoschisis varying in degree It may be mentioned that our series includes the only homozygous female case described in the literature and a four month old boy with severe retinoschisis (Fig 2)

The present paper is a preliminary report on the findings in 29 patients with X chromosomal retinoschisis investigated by fluorescein angiography Novotny and Alvis 1961)

On the basis of the clinical findings the series may be classified as follows

1 Mild cases showing only macular involvement
2 Moderate cases showing schisis or veils with retinal holes peripherally in addition to a typical macular finding

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FLUORESCEIN ANGIOGRAPHIC STUDIES ON X-CHROMOSOMAL RETINOSCHISIS

By

U Krause, Birgitta Vainio Mattila, A Eriksson and H Forsius

As a clinical entity juvenile retinoschisis was described for the first time in 1932 by both Thomson and Andersson Sorsby, in 1951, found that the disease is recessively inherited via the X-chromosome This has later been confirmed in several investigations (e g Vainio Mattila *et al* 1969) As regards the histology of the disease, it was assumed that splitting of the retina in the ganglion cell layer is involved (Levy 1952, François *et al* 1963) This theory was conclusively proved correct in 1968, by Yanoff *et al*, who studied an enucleated eye The histological difference between X-chromosomal retinoschisis and autosomal hyaloid retinal degeneration described by Bohringer *et al* (1960) is thus clear Amalric (1968) investigated angiographically a case of retinoschisis without discussing the heredity His findings were indicative of markedly dystrophic changes in the choroid Using the same technique, Lemke, Jutte and Scheibe (1968) clearly demonstrated the presence of vascular veils The relevant literature has recently been surveyed by Bengtsson and Linder (1967)

The pathological process is sometimes limited to the macula, which in young patients shows a wheel-like formation with radiate folding (Fig 1), due to cystic degeneration of the innermost retinal layer Independently of the macular process, peripherally or nearer the papilla the elevated inner retinal layer may form a veil extending towards the vitreous, as a rule temporally below The findings in the two eyes are often, though not invariably, symmetrical In some cases the veil forms a roll towards the vitreous (Fig 10) Sheathing of retinal vessels is frequently seen peripherally and round the papilla, and haemorrhages have been observed (Bengtsson and Linder 1967) These may also involve the vitreous Anomalies of the papilla, e g in the form of pseudopapillitis, optic atrophy and drusen, have been described by many authors (Levy 1952, Forsius *et al* 1962) The choroid exhibits various degrees of degeneration (Sorsby 1951, Forsius *et al* 1962, 1963) and sclerosis, associated with changes in



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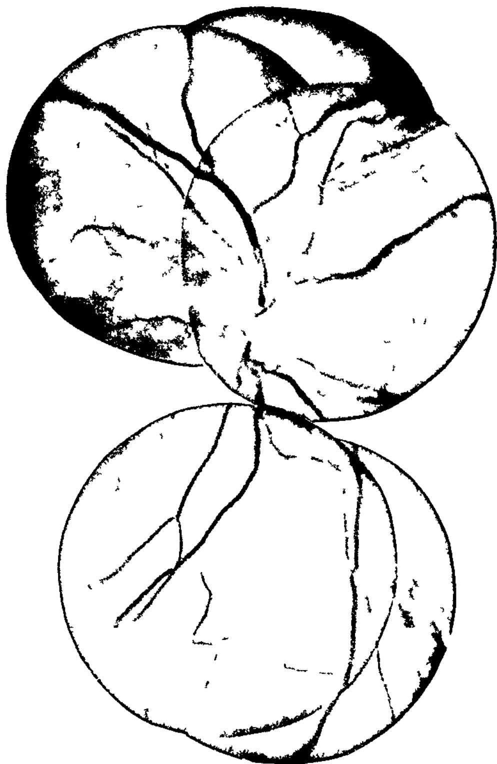


Fig 2
Severe retinoschisis in a boy aged 4 months Only a small sector of the retina (from 8 o clock to 10 o clock) is intact

3 Severe cases showing schisis extending to the vicinity of the papilla and/or other severe anomalies involving the papilla, vessels or vitreous

We have come to the conclusion that as defined above, or in other words in regard to type or form, the disease remains the same throughout life, although within the above mentioned groups the course is slowly progressive so that probably all patients finally lose word vision

In general ordinary black white photography reveals the pathological changes in the macula more clearly than colour photography or even ophthalmoscopy in red free light

In Fig 3A (case 1) the slightest macular changes in the series may be studied There is only a suggestion of a wheel like formation This patient has a visual acuity of 0 5 The angiogram (Fig 3B) shows an intact pigment epithelium in the macular region, without fluorescent areas The next ordinary black white photograph (case 2, Fig 4A) shows a definite wheel like formation in the macula and perimacular radiate streaks As compared to the first case (Fig 3A), the process is more advanced but nonetheless the patient has a visual acuity of 1 0 The angiogram (Fig 4B) displays a normal macula but nasally there is a certain patchiness due to slight atrophy of the retinal pigment epithelial layer

Patient No 3 has a visual acuity of 0 7 The ordinary black white photograph (Fig 5A) shows a patchy macula with a slight indication of a wheel like formation and perimacular radiate folding in the retina The macular pigment epithelium is in part destroyed and the underlying fluorescent choroid shows through (Fig 5B) In all other cases in our series destruction of the pigment epithelium is associated with a visual acuity under 0 1

In case 4 vision is finger counting 4 5 m The ordinary black white photograph (Fig 6A) reveals coarsely granular destruction in the macular region and in the angiogram (Fig 6B) the depigmented areas show clearly through The next series of pictures (case 5) demonstrates the purely macular process in a 68 year old patient whose vision is finger counting 3 5 m On the ordinary black white photograph (Fig 7A) a localized process is seen, with pigment spots in the macula and tortuous light zones which seem to extend outside the macular region At the beginning of the arterial phase (Fig 7B) a fluorescent ring is discernible round the macula and the light areas appearing on the black white photograph are more conspicuous temporally Five seconds later the fluorescence of the nasal areas predominates (Fig 7C) At this point it is difficult to interpret the angiographic finding These pictures show the